2016/2017

Top 300 Pharmacy Drug Cards

The best and easiest way to learn essential information about the top 300 drugs

Jill Kolesar • Lee Vermeulen

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Introduction

The selection of the most commonly prescribed medications was based on a number of reports evaluating medication use based on the number of prescriptions filled in the United States and the cost of those prescriptions.[1-3] Most estimates rely on data from IMS Health, using data from their National Prescription Audit. In addition to these sources, additional information was drawn from a wide range of professional journals to select the most relevant medications to include in this set of cards. Information on medication safety was drawn from multiple sources, but relied on a number of documents maintained by the Institute for Safe Medication Practices (ISMP), which can be found at www.ismp.org. Photographs were taken by the editors at the University of Wisconsin Hospital and Clinics pharmacies, as well as at Target Pharmacy in Madison, Wisconsin. Products with generic versions available in the US market have a representative generic product pictured. Brand name products are generally pictured if a generic version is not yet available in the United States.

It should be noted that these cards include multiple agents in some drug classes, and the information on those cards is very similar. While redundancy is considered a flaw in textbooks and other educational material, repeating information in these crowded classes of drugs is essential for the successful use of flash cards as a learning tool.

1. Brooks M. Top 100 Selling Drugs of 2013. 2014, Jan 30. Medscape. Available at http://www.medscape.com/viewarticle/820011#1. Accessed November 29, 2014.

2. Barthalow M. Top drugs of 2013. *Drug Topics*. Available at http://www.pharmacytimes.com/publications/issue/2014/July2014/Top-Drugs-of-2013. Accessed November 29, 2014.

3. Schumock GT, Li EC, Suda KJ, Matusiak LM, Hunkler RJ, Vermeulen LC, Hoffman JM. National trends in prescription drug expenditures and projections for 2014. *Am J Health Syst Pharm.* 2014;71(6):482-499.

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Preface A: Anatomy of a Flash Card

Medication Name

Both generic and common brand names are listed.

Class

Medications are grouped into classes ("families") based on their chemical, pharmacological, or clinical properties. It is often useful to study medications on a class-by-class basis, identifying similarities and differences among members of each class.

Controlled Substance Schedule

Title 21 of the United States Code (USC) is the Controlled Substances Act of 1970. It regulates medications with potential for abuse. These Federal regulations are overseen by the Drug Enforcement Administration, but many States have enacted more strict regulations based on them. Medications are placed into schedules based on their clinical use and their risk of abuse and dependence. It is important to note that some States change the Federal scheduling of certain medications. Under Federal law, a State cannot place a medication in a lower schedule than where it is placed by the Federal government (eg, States cannot change a drug placed in Federal Schedule II to Schedule III, IV, or V), but States can and do place certain medications in higher schedules (eg, changing a drug placed in Federal Schedule V into Schedule II, III, or IV, or changing a drug which is not a controlled substance under Federal law into a controlled substance within that State).

- *Schedule I:* No medical use, high abuse, and dependence potential.
- *Schedule II:* Legitimate medical use, high abuse, and dependence potential.
- *Schedule III:* Legitimate medical use, abuse, and dependence potential somewhat less than Schedule II.
- *Schedule IV:* Legitimate medical use, abuse, and dependence potential less than Schedule III.
- *Schedule V:* Legitimate medical use, limited abuse, and dependence potential.

Dosage Forms

The most common dosage forms and strengths are listed. Other dosage forms may exist, and may be referenced in the Clinical Pearls section.

Common FDA Label Indication, Dosing, and Titration

The US Food and Drug Administration (FDA) approves medications for market, and also approves specific indications for use and the doses for those uses. Some medications are approved for only one indication, while others are approved for many indications. In most cases, all FDA-approved ("labeled") indications are listed with their approved doses.

Off-Label Uses

While every medication must be approved by the FDA for at least one indication before it is marketed, FDA approval is not always sought for subsequent indications. Prescribers are legally entitled to prescribe medications for any indication they feel is appropriate and clinically justified. In most cases, prescribers limit their use of medications to indications for which evidence supports safety and efficacy, as demonstrated in published clinical trials. While these may not be FDA-approved indications, "off-label" use is common and often completely appropriate. Common off-label uses are included, along with dosing recommendations.

MOA (Mechanism of Action)

The MOA is a succinct summary of the pharmacological properties of each medication.

Drug Characteristics

Each card includes a table summarizing key drug parameters, as outlined below.

Dose Adjustments Hepatic

A Child-Pugh Score can be used to assess hepatic dysfunction. The score employs five clinical measures of liver disease. Each is scored 1-3, with 3 indicating the most severe derangement of that measure. Based on the number of points for each measure, liver disease can be classified into Child-Pugh class A, B, or C.

Measure	1 Point	2 Points	3 Points
Total bilirubin, mg/dL	<2	2-3	>3
Serum albumin, g/L	>35	28-35	<28
INR	<1.7	1.71-2.20	>2.20
Ascites	None	Mild	Severe
Hepatic encephalopathy	None	Grade I-II	Grade III-IV

Points	Class	One-Year Survival	Two-Year Survival	Liver Dysfunction
5-6	A	100%	85%	Mild
7-9	B	81%	57%	Moderate
10-15	C	45%	35%	Severe

Dose Adjustments Renal

Dose adjustments for some (but not all) of medications that are renally eliminated are necessary in patients with renal dysfunction and hepatically eliminated medications in patients with hepatic dysfunction. Dose adjustments are made by either lowering the dose or dosing less frequently (eg, reducing from tid to daily dosing). The degree of renal dysfunction usually determines the degree of the dose adjustment. Definitions of renal and hepatic dysfunction are often inconsistent, but the recommended dose adjustments included in these flash cards are drawn from product package inserts and other sources. Clinicians should always exercise caution when treating patients with liver and/or kidney disease, and monitor carefully for signs of toxicity, even if dose adjustments are made.

In general, CrCl is used to assess renal function and is calculated with the following equations:

Cockcroft and Gault Equation:
CrCl (males) = [(140 – age) × IBW]/(Scr × 72)
CrCl (females) = [(140 – age) × IBW]/(Scr × 72) × (0.85)

Estimate Ideal Body Weight in (kg):
Males: IBW = 50 kg + 2.3 kg for each inch over 5 ft
Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 ft

Normal Renal Function: CrCl = 50 mL/min or greater
Moderate Renal Impairment: CrCl = 30-50 mL/min
Severe Renal Impairment: CrCl =10-29 mL/min
Renal Failure: CrCl = 9 mL/min or less

Dialyzable

Medications may be removed by peritoneal or hemodialysis, requiring dose adjustments and/or redosing after dialysis to replace drug lost. Many references provide details regarding the dialyzability of drugs, and these cards provide basic adjustment recommendations.

Pregnancy Category

The FDA rates and categorizes medications based on the level of risk of fetal harm that medications pose when taken by pregnant women. While these categories are discrete, it is important to recognize that they are sometimes set on the basis of theoretical risks. Clinical decisions must be made individually, weighing the potential risk to both the pregnant woman and the fetus. The pregnancy category of each medication is provided.

- *Category A:* Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
- *Category B:* Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

- *Category C:* Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- *Category D:* There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- *Category X:* Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

For several years, the FDA has considered changes to the pregnancy and lactation risk rating systems, and while the old systems remains in place at the time these cards are being edited, they may change before the next edition is published. Information about the change can be found at the FDA web site, and excellent information about this situation can be found in these two papers: Ramoz LL, Patel-Shori, NM. Recent changes in pregnancy and lactation labeling: Retirement of risk categories. *Pharmacotherapy* 2014;34(4):389-395, and Singh A, Hughes GJ, Mazzola, N. New changes in pregnancy and lactation labeling. *US Pharm.* 2014;39(10):40-43.

Lactation

As with pregnancy categories, relatively little evidence is available to guide clinical decision making regarding the use of medications in women who are breast-feeding. In most cases, the risks to the child must be weighed against the benefits to the breast-feeding mother. In general, this assessment is based on the risk that an individual medication will be expressed in breast milk, and the risk that such an expression would cause to the infant who subsequently ingests it. As noted above, the FDA is considering changes to the pregnancy and lactation systems used to describe risk. The articles cited can be reviewed for information about this pending change.

Contraindications

Some medications should never be used in certain circumstances or under certain conditions. These situations are known as contraindications and are usually related to common and very dangerous adverse effects that must be avoided by selecting alternative therapeutic options.

Absorption

Pharmacokinetic parameters related to oral bioavailability (F) and the impact of food on absorption are provided.

Distribution

Pharmacokinetic data on extent and nature of distribution, including volume of distribution (Vd) and the extent of protein binding, are provided.

Metabolism

Pharmacokinetic data on metabolic pathways, including cytochrome P450 pathway of elimination and whether a drug is an enzyme inducer or inhibitor, are provided.

Elimination

Pharmacokinetic data on extent of renal (or other) elimination, as well as elimination half-life, are provided.

Pharmacogenetics

Pharmacogenetic information is included if the drug has pharmacogenetic information in the drug label. Generally, information is provided when a patient's genetic composition can affect drug exposure and clinical response variability, risk for adverse events, genotype-specific dosing, or mechanism of drug action. A complete list of drugs with pharmacogenetic information can be found at the following web site: http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm.

Black Box Warnings

The FDA requires manufacturers to list certain significant safety-related concerns in boxed warnings in their approved product package inserts. These "black box warnings" contain critical information for the safe use of those medications. Key black box warning content is included on each card. Additional information on black box warnings can be found at the following web site: https://blackboxrx.com/app/index.

Medication Safety Issues

Each card includes a table summarizing key medication safety concerns, as outlined as follows.

Suffixes

Many products are available in multiple formulations, for example, in delayed-release dosage forms. These dosage forms are often distinguished through the use of suffixes appended to the name of a different formulation of that same product. It is essential to exercise caution to avoid errors caused by confusing one product with another by omitting or not recognizing the additional suffix. Products that are available in multiple formulations, distinguished by a suffix (or occasionally, a prefix), are noted in this field.

"Tall Man" Letters

Many medications are spelled similarly, leading to substitution errors during prescribing, dispensing, or administration. The use of "Tall Man" lettering—distinguishing one medication from a different, similarly named medication, by capitalizing specific portions of the medication name (either brand or generic name)—has been shown to help prevent substitution errors. Those products for which Tall Man lettering is recommended are noted in this field.

Do Not Crush

Many solid oral dosage formulations are developed to release their active ingredient slowly over time. Crushing those dosage forms (eg, to enable administration through a nasogastric tube, or to make easier to swallow by patients with swallowing disorders) may be particularly dangerous. The formulations of certain products that should not be crushed are noted in this field. Sublingual dosage forms are meant to be dissolved under the tongue and swallowing these dosage forms without allowing them to dissolve lowers the efficacy of the drug. Some taste really bad, and patients prefer to swallow them without allowing them to dissolve.

High Alert

The Institute for Safe Medication Practices (ISMP) maintains a list of medications that are often involved in medication errors, or that are associated with a heightened risk of causing significant patient harm when used in error. Specific care must be exercised when prescribing, dispensing, or administering these products. More information on this field can be found at the ISMP web site at www.ismp.org.

Confused Names

Many medications are confused with other medications based on similarities in the spelling or pronunciation of their names, resulting in substitution errors. Those products that may be confused with different "look-alike or sound-alike" products are noted in this field.

Beers Criteria

The initial Beers Criteria identified medications for which risks outweigh benefits and those that should be avoided or used with caution in adults aged 65 and older. The list was first published in 1991 by Mark Beers, MD (Beers MH, Ouslander JG, Rollingher I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Int Med.* 1991;151:1825–1832). The list has been revised several times subsequently, most recently by the American Geriatrics Society in 2012 (American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60:616–631). In this version of these drug cards, only warnings included in the first Table 1 of the Beers Criteria, "Agents Potentially Inappropriate Medication Use in Older Adults," have been noted. Two other tables, listing drugs to be used with caution due to drug-disease or drug-syndrome interactions and drugs to be used with caution in older adults, are also included in the Beers guideline, but have not been noted in these cards.

Drug Interactions

Concurrent use of multiple medications (poly-pharmacy) introduces significant risks as certain drugs interact with others to create adverse effects. Many interactions are caused when one agent affects the metabolism of another, thereby either increasing the risk of toxicity (when metabolism is decreased) or decreasing efficacy (when metabolism is increased). Examples of drugs that are inhibitors or inducers of the cytochrome P450 system, or are substrates (drugs metabolized by that system), and other metabolic issues, are included in Prefaces H, I, J, and K. Other mechanisms can also result in negative outcomes. The most common interactions are listed in these cards. Note that in many cases, drugs interact in a similar way with entire classes of other drugs, and in those situations, the class of interacting agent is listed. Lists of the agents that are members of those classes are listed in other prefaces in this card set. Since some interactions are unavoidable, strategies for managing some interactions are provided.

Adverse Reactions

Every drug is associated with potential risks. Adverse effects are evaluated based on the frequency with which they occur and the degree of severity of the reaction, if it does occur. Most medications have a few common adverse effects that may or may not be severe enough to limit the use of the medication, and a few that occur rarely, but are very serious. Common adverse

effects (that occur in >10% of patients who take the medication) and less common (that occur in 1-10% of patients) are summarized in these cards. Rare (occurring in <1% of patients) but serious adverse effects are also listed.

Monitoring Parameters—Efficacy and Toxicity

Patients receiving medications should be monitored to ensure that the treatment is achieving its desired outcome without causing adverse effects. Specific efficacy and toxicity monitoring parameters are listed for each medication.

Key Patient Counseling Points

In order for medications to be used effectively and safely, patients must understand their therapies. Key information that patients should be provided with is summarized for each medication.

Clinical Pearls

Clinical information regarding the use of each medication, including place in therapy, is provided in this section. Special alerts from the FDA, which are usually related to adverse reactions that are being evaluated and have not been included in the product package insert, are included here as well.

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Preface B: Weight and Measure Equivalents

Apothecary Weight Equivalents

1 scruple (℈)	= 20 grains (gr)
60 grains (gr)	= 1 dram (ʒ)
8 drams (ʒ)	= 1 ounce (ʒ)
1 ounce (ʒ)	= 480 grains
12 ounces (ʒ)	= 1 pound (lb)

Apothecary Volume Equivalents

60 minims (m)	= 1 fluidram (fl ʒ)
8 fluidrams (fl ʒ)	= 1 fluid ounce (fl ʒ)
1 fluid ounce (fl ʒ)	= 480 minims
16 fluid ounces (fl ʒ)	= 1 pint (pt)

Avoirdupois Equivalents

1 ounce (oz)	= 437.5 grains
16 ounces (oz)	= 1 pound (lb)

Weight/Volume Equivalents

1 mg/dL	= 10 µg/mL
1 mg/dL	= 1 mg%
1 ppm	= 1 mg/L

Conversion Equivalents

1 gram (g)	= 15.43 grains
1 grain (gr)	= 64.8 milligrams
1 ounce (℥)	= 31.1 grams
1 ounce (oz)	= 28.35 grams
1 pound (lb)	= 453.6 grams
1 kilogram (kg)	= 2.2 pounds
1 milliliter (mL)	= 16.23 minims
1 minim (m)	= 0.06 milliliter
1 fluid ounce (fl oz)	= 29.57 mL
1 pint (pt)	= 473.2 mL
0.1 mg	= 1/600 gr
0.12 mg	= 1/500 gr
0.15 mg	= 1/400 gr
0.2 mg	= 1/300 gr
0.3 mg	= 1/200 gr
0.4 mg	= 1/150 gr
0.5 mg	= 1/120 gr
0.6 mg	= 1/100 gr
0.8 mg	= 1/80 gr
1 mg	= 1/65 gr

Preface C: General Content Related to All Oral Contraceptives

MOA. As contraceptives, estrogens suppress follicle-stimulating hormone (FSH) and luteinizing hormone (LH) to inhibit ovulation, cause edematous endometrial changes that are hostile to implantation of the fertilized ovum, accelerate ovum transport, and produce degeneration of the corpus luteum (luteolysis). Progestins inhibit ovulation by suppression of LH, inhibit sperm capacitation, slow ovum transport, produce a thinning endometrium that hampers implantation, and cause cervical mucus changes that are hostile to sperm migration.

Pharmacokinetics of Progestins

Agent	Absorption	Distribution	Metabolism	Elimination
Norgestrel	Unknown	Unknown	Unknown	Unknown
Norethindrone	F = 64%; food has no effect on absorption	Vd = 4 L/kg; highly protein bound	Hepatic not via CYP450	Renal elimination with a half-life of 8 h
Drospirenone	F = 76-85%; food has no effect on absorption	Vd = 4.2 L/kg; highly protein bound	Hepatic not via CYP450	Renal elimination is 38-47% with a half-life of 36-42 h
Desogestrel	F = Almost 100%; food has no effect on absorption	Unknown	Hepatic via CYP2C9 to active metabolite, etonogestrel	Renal elimination of etonogestrel 45% with a half-life of 37 h
Levonorgestrel	F = 100%; food has no effect on absorption	Vd = 1.8 L/kg; highly protein bound	Hepatic not via CYP450	Renal elimination is 45% with a half-life of 17-27 h

Drug Interactions: Oral Contraceptives

Typical Agents	Mechanism	Clinical Management
CYP1A2 substrates	Contraceptives inhibit CYP1A2-mediated metabolism, resulting in increased substrate concentrations and toxicity	Avoid or monitor and reduce substrate dose as needed
CYP2C8 substrates	Contraceptives inhibit CYP2C8-mediated metabolism, resulting in increased substrate concentrations and toxicity	Avoid or monitor and reduce substrate dose as needed
CYP3A4/5 inducers	Increased contraceptive metabolism reduces contraceptive effectiveness	Use an alternative form of birth control
CYP3A4/5 inhibitors	Decreased contraceptive metabolism increases risk of contraceptive toxicity	Monitor for toxicity and discontinue contraceptive if necessary
CYP3A4/5 substrates	Competitive inhibition of CYP3A4/5 metabolism of other CYP3A4/5 substrates	Monitor for adverse effects and reduce substrate dose as necessary
Antibiotics	Alters intestinal flora which, in turn, reduces the enterohepatic circulation of estrogen metabolites resulting in decreased efficacy of contraceptive	Use an alternative form of birth control
Corticosteroids	Corticosteroid metabolism inhibited by the contraceptive resulting in toxicity	Monitor for corticosteroid toxicity and reduce dose if necessary
Warfarin	Contraceptive may increase or decrease warfarin effectiveness; mechanism unknown	Carefully monitor INR

Adverse Reactions: Oral Contraceptives

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight change, breast tenderness, breast swelling	Bloating, nausea, stomach cramps, vomiting, depression	Arterial thromboembolism, myocardial infarction, thrombophlebitis, cerebral hemorrhage, cerebral thrombosis, pulmonary embolism, hypertension

Key Patient Counseling Points. Hormonal contraceptives do not protect against HIV infection or other sexually transmitted diseases. Take this drug at approximately the same time each day. If spotting occurs and no doses have been missed, continue to take tablets even if spotting continues. Report immediately if new severe or persistent headache; blurred or loss of vision; shortness of breath; severe leg, chest, or abdominal pain; or any abnormal vaginal bleeding occur. If you miss 1 dose, take it as soon as you remember it and take the next tablet at the correct time even if you take 2 tablets on the same day or at the same time. If you miss 2 doses in week 1 or 2, take 2 tablets on the day you remember and 2 tablets the next day. If you miss 2 doses in week 3 or miss 3 or more active tablets, then (if you start on day 1) start a new pack the same day or (if you start on Sunday) take 1 tablet daily until Sunday and then start a new pack that day. Use an alternative form of contraception for the next 7 d after you miss 2 or more doses in weeks 1, 2, or 3.

Clinical Pearls. Patients with thrombogenic mutations (eg, factor V Leiden) should not receive oral contraceptives. The CDC provides recommendations for choice of oral contraceptives on their web site at www.cdc.gov. Age, cigarette smoking, concurrent diseases, weight, drug interactions, and reproductive status are all considered when selecting a contraceptive regimen.

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Blood Pressure Lowering Therapies

Complete JNC-8 guidelines available at http://jama.jamanetwork.com/article.aspx?articleid=1791497.

Hypertension Guideline Management Algorithm

Adults Aged ≥18 y With HTN (JNC-8)	Systolic BP Goal (mm Hg)	Diastolic BP Goal (mm Hg)	Initial Treatment Recommendation: Nonblack Patients	Initial Treatment Recommendation: Black Patients
Age ≥60 y without DM or CKD	<150	<90	LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination	LSM + thiazide-type diuretic or CCB, alone or in combination
Age <60 y without DM or CKD	<140	<90	LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination	LSM + thiazide-type diuretic or CCB, alone or in combination
All ages with DM and no CKD	<140	<90	LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination	LSM + thiazide-type diuretic or CCB, alone or in combination
All ages with CKD with or without DM	<140	<90	LSM + ACE-I or ARB, alone or in combination with other drug class	LSM + ACE-I or ARB, alone or in combination with other drug class

ACE-I = ACE inhibitor
ARB = Angiotensin receptor blocker
BP = Blood pressure
CCB = Calcium channel blocker
CKD = Chronic kidney disease
DM = Diabetes mellitus
LSM = Lifestyle modifications, including weight reduction, limit alcohol, aerobic activity, limit sodium intake, tobacco cessation, DASH diet

Strategies to Dose Antihypertensive Therapy

A—Start with 1 drug; titrate to maximum recommended dose to achieve goal BP. Add 2nd drug from list (thiazide-type diuretic, CCB, ACE-I, or ARB)* if goal BP not achieved after titration; titrate 2nd drug to maximum recommended dose to achieve goal BP. If goal BP not reached with 1 drugs, add 3rd agent from list and titrate to maximum recommended dose to achieve BP goal. *AVOID combination of ACE-I and ARB*.
B—Start with 1 drug; if goal BP not reached, add 2nd drug from list before achieving maximum recommended dose with 1st drug. Titrate both drugs to maximum recommended doses to achieve BP goal. If goal BP not reached with 2 drugs, add 3rd drug from list and titrate to maximum recommended dose to achieve BP goal. *AVOID combination of ACE-I and ARB*.
C—Initiate therapy with 2 drugs when SBP >160 mm Hg and/or DBP is >100 mm Hg (or if SBP >20 mm Hg and/or DBP >10 mm Hg above goal), either as 2 separate drugs or single combination tablet/capsule. If goal BP not achieved with 2 drugs, add 3rd drug from list and titrate 3rd drug to maximum recommended dose. *AVOID combination of ACE-I and ARB*.

*List reflects those classes of antihypertensive drugs that have demonstrated improved outcomes in randomized controlled trials; drugs from other antihypertensive categories may also be considered.

Evidence-Based Dosing for Antihypertensive Medications

Medication	Initial Daily Dose (mg)	Number of Doses per Day	Target Dose (mg)
ACE inhibitors			
Captopril	50	2	150-200
Enalapril	5	1-2	20
Lisinopril	10	1	40
Angiotensin receptor blockers			
Candesartan	4	1	12-32
Irbesartan	75	1	300
Losartan	50	1-2	100
Valsartan	40-80	1	160-320
Beta-blockers			
Atenolol	25-50	1	100
Metoprolol	50	1-2	100-200
Calcium channel blockers			
Amlodipine	2.5	1	10
Diltiazem extended release	120-180	1	360
Thiazide-type diuretics			
Chlorthalidone	12.5	1	12.5-25
Hydrochlorothiazide	12.5-25	1-2	25-50
Indapamide	1.25	1	1.25-2.5

Antihypertensive Drug Classif cations

Class	Commonly Used Drugs
ACE inhibitors	Benazepril Captopril Enalapril Fosinopril Lisinopril Moexipril Perindopril Quinapril Ramipril Trandolapril
Aldosterone antagonists	Eplerenone Spironolactone
α_1-Blockers	Doxazosin Prazosin Terazosin
Angiotensin receptor blockers	Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan

Beta-blockers: nonselective	Betaxolol Nadolol Propranolol Propranolol long acting Timolol
Beta-blockers: cardiac selective	Atenolol Bisoprolol Metoprolol succinate Metoprolol tartrate Nebivolol
Beta-blockers: intrinsic sympathomimetic activity	Acebutolol Penbutolol Pindolol
Combined alpha- and beta-blockers	Carvedilol Labetalol
Calcium channel blockers: dihydropyridines	Amlodipine Felodipine Isradipine Nicardipine sustained release Nifedipine sustained release Nisoldipine
Calcium channel blockers: non-dihydropyridines	Diltiazem extended release Verapamil Verapamil long acting

Centrally acting agents	Clonidine Clonidine patch Guanfacine Methyldopa Reserpine
Direct renin inhibitor	Aliskiren
Direct vasodilators	Hydralazine Minoxidil
Diuretics: thiazides	Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone
Diuretics: loops	Bumetanide Furosemide Torsemide
Diuretics: potassium sparing	Amiloride Triamterene

Cholesterol Management

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults available at http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.

Cardiovascular Risk Calculator available at http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp.

Cholesterol Treatment Recommendations to Reduce Atherosclerotic Cardiovascular Disease (ASCVD) Risk in Adults

Patient Population		Recommended Treatment (Heart-healthy lifestyle habits are recommended for all patients)
Diagnosed with clinical ASCVD* (secondary prevention)	Age 21-75 y and no statin safety concerns	High-intensity statin
	Age >75 y or statin safety concerns (conditions or drug-drug interactions affecting statin safety or history of statin intolerance)	Medium-intensity statin
LDL-C ≥190 mg/dL (primary prevention)	Age ≥21 y	High-intensity statin; if goal LDL-C lowering not achieved, may add nonstatin therapy to achieve >50% reduction in LDL-C
Diabetes and LDL-C 70-189 mg/dL (primary prevention)	Age 40-75 y	Moderate-intensity statin If 10-y ASCVD risk ≥7.5%: high-intensity statin
No diabetes and LDL-C 70-189 mg/dL (primary prevention)	Age 40-75 y	10-y ASCVD risk ≥7.5%: moderate- to high-intensity statin 10-y risk 5 to <7.5%: moderate-intensity statin

*Clinical ASCVD includes: acute coronary syndromes, history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral arterial disease.

Recommended Statin Intensity to Reduce ASCVD Risk

Low-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	High-Intensity Statin Therapy
Daily dose lowers LDL-C on average by <30%	Daily dose lowers LDL-C on average by approximately 30% to <50%	Daily dose lowers LDL-C on average by approximately ≥50%
Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg

Cholesterol-Lowering Drugs

Class	Drugs	Average Effects on Lipoproteins	Adverse Effects
Bile acid sequestrants	Cholestyramine Colesevelam Colestipol	HDL-C ↑ 3-5% TG No change to ↑ 9% LDL-C ↓ 15-30%	Abdominal discomfort and cramping, constipation, flatulence, nausea/vomiting, vitamin deficiency
Cholesterol absorption inhibitor	Ezetimibe	HDL-C ↑ 1% TG ↓ 8% LDL-C ↓ 18%	Arthralgia, diarrhea, myalgia
Fibric acid	Fenofibric acid Fenofibrate Gemfibrozil	HDL-C ↑ 10-20% TG ↓ 20-50% LDL-C ↓ 5-20%	Abdominal pain, arthralgia, constipation, diarrhea, headache, increased liver enzymes, indigestion, myalgia, myopathy, nausea, rhabdomyolysis
HMG-CoA reductase inhibitors (statins)	Atorvastatin Fluvastatin Fluvastatin XL Lovastatin Pitavastatin Pravastatin Rosuvastatin Simvastatin	HDL-C ↑ 5-15% TG ↓ 7-30% LDL-C ↓ 18-55%	Arthralgia, diarrhea, headache, increased liver enzymes, indigestion, insomnia, myalgia, myopathy, nausea, rhabdomyolysis
Nicotinic acid	Niaspan	HDL-C ↑ 15-35% TG ↓ 20-50% LDL-C ↓ 5-25%	Flushing, pruritus, rash, nausea/vomiting, increased glucose levels, increased liver enzymes, myalgia, myopathy
Omega-3–acid ethyl ester	Vascepa (EPA)	TG ↓ 21-27%	Joint pain, sore throat
Omega-3–acid ethyl esters	Lovaza (EPA/DHA)	HDL-C ↑ 9% TG ↓ 45% LDL-C ↓ 45%	Altered taste, burping, indigestion, pruritus, rash

HMG-CoA Reductase Inhibitors Comparison

Statin Drug	Dose (mg/d)	%Change on Lipoproteins		
		LDL-C	TG	HDL-C
Atorvastatin	10-80	↓ 39-60	↓ 19-37	↑ 5-9
Fluvastatin	20-80	↓ 22-36	↓ 12-25	↑ 3-11
Lovastatin	10-80	↓ 24-40	↓ 10-19	↑ 7-10
Pitavastatin	1-4	↓ 31-45	↓ 13-22	↑ 1-8
Pravastatin	10-80	↓ 22-37	↓ 11-24	↑ 2-12
Rosuvastatin	5-40	↓ 45-63	↓ 10-35	↑ 8-14
Simvastatin	5-80*	↓ 26-47	↓ 12-33	↑ 8-16

*80-mg dose restricted to patients who have been taking it for more than 12 mo without evidence of myopathy

Hypertension

Combination Type	Fixed Dose Combination (mg)	Trade Name
ACE inhibitor and CCB	Amlodipine-benazepril (2.5/10, 5/10, 5/20, 10/20) Enalapril-felodipine (5/5) Trandolapril-verapamil (2/180, 1/240, 2/240, 4/240)	Lotrel Lexxel Tarka
ACE inhibitor and diuretic	Benazepril- HCTZ (5/6.25, 10/12.5, 20/12.5, 20/25) Captopril-HCTZ (25/15, 25/25, 50/15, 50/25) Enalapril-HCTZ (5/12.5, 10/25) Fosinopril-HCTZ (10/12.5, 20/12.5) Lisinopril-HCTZ (10/12.5, 20/12.5, 20/25) Moexipril-HCTZ (7.5/12.5, 15/25) Quinapril-HCTZ (10/12.5, 20/12.5, 20/25)	Lotensin HCT Capozide Vaseretic Monopril/HCT Prinzide, Zestoretic Uniretic Accuretic
ARB and CCB	Amlodipine-olmesartan (5/20, 5/40, 10/20, 10/40) Amlodipine-telmisartan (5/40, 5/80, 10/40, 10/80) Amlodipine-valsartan (5/160, 5/320, 10/160, 10/320)	Azor Twynsta Exforge
ARB and CCB and diuretic	Amlodipine-HCTZ-olmesartan (5/12.5/20, 5/12.5/40, 5/25/40, 10/12.5/40, 10/25/40) Amlodipine-HCTZ-valsartan (5/12.5/160, 5/25/160, 10/12.5/160, 10/25/160, 10/25/320)	Tribenzor Exforge HCT

ARB and diuretic	Azilsartan-chlorthalidone (40/12.5, 40/25) Candesartan-HCTZ (16/12.5, 32/12.5) Eprosartan-HCTZ (600/12.5, 600/25) Irbesartan-HCTZ (150/12.5, 300/12.5) Losartan-HCTZ (50/12.5, 100/25) Olmesartan medoxomil-HCTZ (20/12.5, 40/12.5, 40/25) Telmisartan-HCTZ (40/12.5, 80/12.5) Valsartan-HCTZ (80/12.5, 160/12.5, 160/25)	Edarbyclor Atacand HCT Teveten-HCT Avalide Hyzaar Benicar-HCT Micardis-HCT Diovan-HCT
BB and diuretic	Atenolol-chlorthalidone (50/25, 100/25) Bisoprolol-HCTZ (2.5/6.25, 5/6.25, 10/6.25) Metoprolol succinate-HCTZ (25/12.5, 50/12.5, 100/12.5) Metoprolol tartrate-HCTZ (50/25, 100/25) Nadolol-bendroflumethiazide (40/5, 80/5) Propranolol LA-HCTZ (40/25, 80/25)	Tenoretic Ziac Dutoprol Lopressor HCT Corzide Inderide LA
Centrally acting drug and diuretic	Chlorthalidone-clonidine (15/0.1, 15/0.2, 15/0.3) Methyldopa-HCTZ (250/15, 250/25, 500/30, 500/50) Reserpine-chlorthalidone (0.125/25, 0.25/50) Reserpine-chlorothiazide (0.125/250, 0.25/500) Reserpine-HCTZ (0.125/25, 0.25/50)	Clorpres Aldoril Regroton Diupres Hydropres

Direct renin inhibitor and CCB	Aliskiren-amlodipine (150/5, 150/10, 300/5, 300/10)	Tekamlo
Direct renin inhibitor and diuretic	Aliskiren-HCTZ (150/12.5, 150/25, 300/12.5, 300/25)	Tekturna HCT
Direct renin inhibitor and CCB and diuretic	Aliskiren-amlodipine-HCTZ (150/5/12.5, 300/5/12.5, 300/5/25, 300/10/12.5, 300/10/25)	Amturnide
Diuretic combination	Amiloride-HCTZ (5/50) Spironolactone-HCTZ (25/25, 50/50) Triamterene-HCTZ (37.5/25, 75/50)	Moduretic Aldactazide Dyazide, Maxzide

Lipid Lowering

Combination Type	Fixed Dose Combination (mg)	Trade Name
Statin and cholesterol absorption inhibitor	Ezetimibe-atorvastatin (10/10, 10/20, 10/40, 10/80) Ezetimibe-simvastatin (10/10, 10/20, 10/40, 10/80)	Liptruzet Vytorin
Statin and nicotinic acid	Lovastatin-niacin (20/500, 20/750, 20/1000, 40/1000) Niacin-simvastatin (500/20, 500/40, 750/20, 1000/20, 1000/40)	Advicor Simcor

Hypertension/Lipid Lowering

Combination Type	Fixed Dose Combination (mg)	Trade Name
CCB and statin	Amlodipine-atorvastatin (2.5/10, 2.5/20, 2.5/40, 5/10, 5/20, 5/40, 5/80, 10/10, 10/20, 10/40, 10/80)	Caduet

Glucose Lowering/Lipid Lowering

Combination Type	Fixed Dose Combination (mg)	Trade Name
Statin and dipetidyl peptidase-4 (DDP-4) enzyme inhibitor	Simvastatin-sitagliptin (10/50, 10/100, 20/50, 20/100, 40/50, 40/100)	Juvisync

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Preface G: Guide to Combination Vaccines

Vaccine	Trade Name	Type	Route	Comments
DTaP	Daptacel Infanrix Tripedia	Inactivated bacterial, toxoid	IM	Diphtheria, tetanus, acellular pertussis
DTaP-HepB-IPV	Pediarix	Inactivated bacterial, toxoid, viral	IM	Licensed for doses at 2, 4, and 6 mo of age; can be used through age 6 y
DTaP-IPV	Kinrix	Inactivated bacterial, toxoid, viral	IM	Licensed for 5th dose in series at 4-6 y
DTaP-IPV-Hib	Pentacel	Inactivated bacterial, toxoid, viral	IM	Licensed for 4 doses at 2, 4, 6, and 15-18 mo
Haemophilus influenzae type b-hepatitis B	Comvax	Inactivated bacterial, viral	IM	Not used for birth dose of hepatitis B
Hib-MenCY	MenHibrix	Inactivated bacterial	IM	Licensed for 4 doses at 2, 4, 6, and 12-15 mo of age
Hepatitis A-hepatitis B	Twinrix	Inactivated viral	IM	≥18 y; 3-dose series
Measles-mumps-rubella	MMR-II	Live attenuated viral	SC	Minimum age 12 mo
Measles-mumps-rubella-varicella	ProQuad	Live attenuated viral	SC	Licensed for ages 1-12 y
Tdap	Boostrix Adacel	Inactivated bacterial, toxoid	IM	Tetanus and diphtheria toxoids and pertussis vaccine; ≥10 y of age Tetanus and diphtheria toxoids and pertussis vaccine; 11-64 y of age

IM = intramuscular
SC = subcutaneous

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Preface H: Guide to Cytochrome P450 (CYP) and UGT1A1 Metabolism

Definitions

Inhibitors

- *Strong inhibitor* is one that causes a ≥5-fold increase in the plasma AUC values or >80% decrease in clearance.
- *Moderate inhibitor* is one that causes a ≥2-fold but <5-fold increase in the plasma AUC values or 50-79% decrease in clearance.
- *Weak inhibitor* is one that causes a >1.25-fold but <2-fold increase in the plasma AUC values or 20-49% decrease in clearance.

Inducers

- *Strong inducer* is one that causes a ≥80% decrease in the plasma AUC.
- *Moderate inducer* is one that causes a 50-79% decrease in plasma AUC.
- *Weak inducer* is one that causes a 20-49% decrease in plasma AUC.

Substrates

- *Sensitive substrates* are when ≥25% of metabolism occurs via a given enzyme.
- *Non-sensitive substrates* are when <25% of metabolism occurs via a given enzyme.

Clinical Implications

Assessment and clinical management of drug-drug interaction:

1. Are both drugs systemically absorbed? If no, no drug interaction.
2. Do both drugs impact the same enzyme system? If not, no drug interaction.
3. The majority of clinically significant drug interactions involve and enzyme inducer or inhibitor and a sensitive substrate (which is metabolized by the enzyme). For example, itraconazole is a strong inhibitor of CYP3A4/5. Amiodarone is a sensitive substrate. Giving them together may result in higher amiodarone levels and toxicity. Clinical management would be to select an alternative antifungal, of dose reduce amiodarone. Strong inducers increase metabolism and decrease efficacy of substrates. Clinical management would be to select an alternative agent or increase the dose of the substrate.

4. Some drugs are prodrugs and require an enzyme to be activated. For example, itraconazole is a strong inhibitor of CYP3A4/5. Cyclophosphamide is a sensitive substrate that is converted to its active metabolite, acrolein, by CYP3A4/5. Giving them together may result in lower acrolein levels and loss of efficacy. Clinical management would be to select an alternative antifungal. Strong inducers, like carbamazepine, increase metabolism and have higher acrolein levels. Clinical management would be to select an alternative agent or decrease the dose of the cyclophosphamide.

Note: Only strong and moderate inhibitors and inducers are included in the drug interaction and drug fact sections. Weak inhibitors and inducers are unlikely to be clinically significant.

CYP1A2

Inhibitors (Strong). Caffeine, ciprofloxacin, enoxacin, fluvoxamine, ketoconazole, lidocaine, methoxselan, mexilitine, norfloxacin, ofloxacin, primaquine, thiabendazole

Inhibitors (Moderate). Amlodipine, cimetidine, diclofenac, fluoxetine, fospropofol, gemfibrozil, miconazole, nifedipine, propofol, zileuton

Inducers. Aminoglutethimide, carbamazepine, phenobarbital, primadone, rifampin

Substrates (Sensitive). Acenocoumarol, aminophylline, betaxolol, caffeine, clomipramine, clozapine, cyclobenzaprine, dacarbazine, doxepin, duloxetine, estrogens, flutamide, fluvoxamine, mexiletine, mirtazapine, pimozide, propranolol, riluzole, ropinorole, tacrine, theophylline, thiothixene, trifluoperazine

CYP2A6

Inhibitors (Strong). Letrozole, methoxselan, miconazole, tranlcypromine

Inhibitors (Moderate). Amiodarone, desipramine, isoniazid, ketoconazole

Inducers. Amobarbital, pentobarbital, phenobarbital, rifampin, secobarbital

Substrates (Sensitive). Dexmedetomidine

CYP2B6

Inhibitors (Strong). None

Inhibitors (Moderate). Doxorubicin, paroxetine, sorafenib

Inducers. Carbamazepine, phenobarbital, phenytoin, rifampin

Substrates (Sensitive). Bupropion, cyclophosphamide (activated to acrolein by CYP2B6), efavirenz, irinotecan, ketamine, promethazine, propofol, selegiline

CYP2C8

Inhibitors (Strong). Atorvastatin, gemfibrozil, ritonavir

Inhibitors (Moderate). Celecoxib, felodipine, fenofibrate, irbesartan, losartan, pioglitazone, quine, rabeprazole, rosiglitazone, tamoxifen, trimethoprim

Inducers. Carbamazepine, phenobarbital, phenytoin, primodone, rifampin, secobarbital

Substrates (Sensitive). Amitriptyline, mestranol (activated by CYP2C8 to ethinyl estradiol), paclitaxel, pioglitazone, rifabutin, rosuvastatin, tretinoin

CYP2C9

Inhibitors (Strong). Delaviridine, flurbiprofen, fluconazole, ibuprofen, indomethacin, isoniazid, mefenamic acid, miconazole, nicardipine, sulfadiazine, sulfisoxazole, tolbutamide

Inhibitors (Moderate). Amiodarone, efavirenz, fenofibrate, fluvastatin, gemfibrozil, irbesartan, ketoconazole, losartan, omeprazole, pantoprazole, pyrimethamine, quinine, sorafenib, sulfamethoxazole, trimethoprim, warfarin, zafirlukast

Inducers. Carbamazepine, phenobarbital, phenytoin, primodone, rifampin, rifapentine, secobarbital

Substrates (Sensitive). Alprazolam, bosentan, carvedilol, celecoxib, dapsone, fluoxetine, glimeride, glipizide, ketamine, losartan, mestranol (activated by CYP2C9 to ethinyl estradiol), montelukast, paclitaxel, phenytoin, propofol, sulfadiazine, sulfamethoxazole, sulfisoxazole, sulfinpyrazone, tamoxifen, tolbutamide, torsemide, trimethoprim, voriconazole, warfarin, zafirlukast, zopiclone

CYP2C19

Inhibitors (Strong). Delaviridine, fluconazole, fluoxetine, fluvoxamine, gemfibrozil, ketoconazole, miconazole, modafinil, omeprazole, piroxicam, ticlopidine

Inhibitors (Moderate). Bortezomib, cimetidine, efavirenz, esomeprazole, fospropofol, lansoprazole, loratadine, nicardipine, propofol, rabeprazole, sertraline

Inducers. Aminoglutethimide, carbamazepine, phenytoin, rifampin

Substrates (Sensitive). Carisoprodol, citalopram, clobazam, clomipramine, diazepam, escitalopram, esomeprazole, imipramine, lansoprazole, methsuximide, moclobemide, nelfinavir, nilutamide, omeprazole, pantoprazole, pentamidine, phenobarbital, phenytoin, progesterone, rabeprazole, ranitidine, sertraline, trimipramine, voriconazole

CYP2D6

Inhibitors (Strong). Chlorpromazine, cinacalet, cocaine, delaviridine, dexmedetomidine, dextromethorphan, fluoxetine, miconazole, paroxetine, pergolide, quinidine, ritonavir, ropinirole, terbinafine, quinine

Inhibitors (Moderate). Amiodarone, chloroquine, cimetidine, clomipramine, clozapine, darifenacin, desipramine, diphenhydramine, duloxetine, haloperidol, imipramine, isoniazid, lidocaine, methadone, methimazole, nicardipine, pioglitazone, pyrimethamine, quinine, ranolazine, sertraline, thioridazine, ticlopidine, trazadone

Inducers. None

Substrates (Sensitive).

- *Antibiotics:* Chloroquine, doxycycline
- *Cardiovascular:* Atorvastatin, betaxolol, captopril, carvedilol, flecainide, lidocaine, metoprolol, mexiletine, pindolol, propafenone, propranolol, timolol
- *CNS:* Amitriptyline, amphetamine, amoxapine, aripiprazole, chlorpromazine, clomipramine, desipramine, dextroamphetamine, dextromethorphan, dihydroergotamine, duloxetine, fluoxetine, flurazepam, fluvoxamine, haloperidol, imipramine, methylphenidate, mirtazapine, moclobemide, nefazodone, nortriptyline, paroxetine, perphenazine, promethazine, risperidone, sertraline, thioridazine, tramadol, trimipramine, venlafaxine
- *Pain:* Codeine (prodrug, activated by CYP2D6 to morphine), oxycodone
- *Oncology:* Doxorubicin, lomustine, tamoxifen
- *Misc:* Hydrocortisone, lansoprazole, tamulosin

CYP2E1

Inhibitors (Strong). Disulfiram

Inhibitors (Moderate). Isoniazid, miconazole

Inducers. None

Substrates (Sensitive). Chlorzoxazone, dacarbazine, halothane, isoflurane, isoniazid, sevoflurane, theophylline, trimethadione

CYP3A4/5

Inhibitors (Strong). Atazanavir, amprenavir/fosamprenavir, clarithromycin, conivaptan, delaviridine, enoxacin, imatinib, indinavir, isoniazid, itraconazole, ketoconazole, miconazole, nefazodone, nelfinavir, nicardipine, propofol, ritonavir, telithromycin

Inhibitors (Moderate). Amiodarone, aprepitant, cimetidine, clotrimazole, desipramine, dexamethasone, diltiazem, doxycycline, erythromycin, fluconazole, isoniazid, lidocaine, metronidazole, miconazole, norfloxacin, sertraline, tetracycline, verapamil, voriconazole

Inducers. Aminoglutethimide, carbamazepine/oxcarbazepine, nevirapine, phenobarbital, phenytoin, pentobarbital/primadone, rifabutin, rifampin

Substrates (Sensitive)

- *Acid blockers:* Cisapride, lansoprazole, omeprazole, rabeprazole
- *Antibiotics:* Chloroquine, clarithromycin, doxycycline, erythromycin, mefloquine, telithromycin, tetracycline, trimethoprim, spiramycin
- *Antifungals:* Itraconazole, ketoconazole, miconazole
- *Antihistamines:* Azelastine, cerivistatin, chlorpheniramine
- *Cardiovascular:* Amiodarone, bosenten, budesonide, cilostazol, diltiazem, disopyramide, enalapril, felodipine, isosorbide, isradipine, lidocaine, losartan, lovastatin, moricizine, nicardipine, nifedipine, nimodipine, nisoldipine, quinidine, simvastatin, ticlodipine
- *CNS:* Alprazolam, amoxapine, benztropine, buprenorphine, buspirone, carisoprodol, clorazepate, chlordiazepoxide, clobazam, clonazepam, cocaine, dantrolene, diazepam, dihydroergotamine, doxepin, eletriptan, escitalopram, ethosuximide, felbamate, flurazepam, haloperidol, mirtazapine, modafinil, pergolide, phencyclidine, pimozide, quetiapine, ranolazine, trazodone, tiagabine, triazolam

- *HIV:* Amprenavir, atazanavir, delavirdine, efavirenz, indinavir, nefazodone, nelfinavir, nevirapine, primaquine, rifabutin, ritonavir, saquinavir, tipranavir
- *Hormones/Steroids:* Estrogens, exemestane, flutamide, fluticasone, letrozole, medroxyprogesterone, mestranol, progesterone, toremifene
- *Immunosuppressants:* Cyclosporine, dapsone, sirolimus, tacrolimus
- *Oncology:* Bortezomib, busulfan, cyclophosphamide (activated to acrolein by CYP3A4/5), docetaxel, doxorubicin, etoposide, ifosfamide (activated to acrolein by CYP3A4/5), imatinib, irinotecan, paclitaxel, sorafenib, sunitinib, teniposide
- *Pain/Sedation:* Alfentanil, fentanyl, ketamine, methadone, midazolam, sufentanil
- *Pulmonary:* Albuterol, montelukast, salmeterol, theophylline
- *Misc:* Aprepitant, brinzolamide, bromocriptine, colchicine, conivaptan, nateglinide, repaglinide, sibutramine, sildenafil, tamsulosin

UGT1A1

Inhibitors

Atazanavir, gemfibrozil, indinavir

Inducers

Carbamazepine

Substrates

Indacaterol, irinotecan, nilotinib, pazopanib, statins

Definitions

Inhibitors

Inhibitors increase the AUC of substrate drugs by ≥1.25-fold.

Inducers

Inducers decrease the AUC of substrate drugs by ≥1.20-fold.

Substrates

- *Sensitive substrates* are when ≥25% of metabolism occurs via a given enzyme.
- *Nonsensitive substrates* are when <25% of metabolism occurs via a given enzyme.

Clinical Implications

Understanding the interaction of drugs with Pgp can assist with managing drug interactions. For example, adding carbamazepine (a Pgp inducer) to digoxin (a Pgp substrate) can lead to marked decreases in serum digoxin concentrations. Clinical management would include monitoring digoxin levels and making dose adjustments.

P-glycoprotein/ABCB1

P-glycoprotein (Pgp) is a membrane-bound, active transport protein located in a number cells and tissues, including intestinal epithelial cells, various lymphocytes, biliary tract, brain, and proximal tubular cells of the kidney. ABCB1 is the name of the gene, while Pgp is the protein.

Its major function is as an efflux transporter of drugs and chemicals. Effects of inducers and inhibitors vary by their location. For example, Pgp transports substrate drugs out of the brain. Inducers may decrease concentrations in the CSF, because there is increased amount of Pgp available to transport substrates, while inhibitors may increase CSF concentrations.

Inhibitors. Abiraterone, amiodarone, atorvastatin, carvedilol, clarithromycin, cobicistat, crizotinib, cyclosporine, darunavir, dipyridamole, dronedarone, erythromycin, grapefruit juice, itraconazole, ivacaftor, ketoconazole, lapatinib, lomitapide, lopinavir, mefloquine, nelfinavir, nicardipine, nilotinib, progesterone, propranolol, quinidine, quinine, ranolazine, reserpine, ritonavir, saquinavir, sunitinib, tacrolimus, tamoxifen, telaprevir, ulipristal, vandetanib, vemurafenib, verapamil.

Inducers. Carbamazepine, dexamethasone, doxorubicin, nefazodone, prazosin, rifampin, St. John's wort, tenofovir, tipranavir, trazodone, vinblastine.

Substrates (Sensitive). Aliskiren, amiodarone, atorvastatin, bosutinib, carfilzomib, carvedilol, cetirizine, cimetidine, ciprofloxacin, colchicine, crizotinib, cyclosporine, dabigatran, daunorubicin, desloratadine, dexamethasone, digitoxin, digoxin, diltiazem, docetaxel, doxorubicin, erythromycin, estradiol, etoposide, everolimus, fexofenadine, fosamprenavir, hydrocortisone, idarubicin, imatinib, indinavir, irinotecan, ivermectin, lapatinib, linagliptin, loperamide, loratadine, lovastatin, methotrexate, mitomycin, nadolol, nelfinavir, nicardipine, ondansetron, paclitaxel, paclitaxel protein bound, paliperidone, pazopanib, pomalidomide, pravastatin, quinidine, quinine, ranitidine, ranolazine, rifampin, risperidone, ritonavir, rivaroxaban, romidepsin, saquinavir, saxagliptin, silodosin, sirolimus, sitagliptin, tacrolimus, telaprevir, temsirolimus, teniposide, tolvaptan, trabectedin, vemurafenib, verapamil, vinblastine, vincristine, vismodegib.

Preface J: Drugs That Affect Cardiac Rhythm

Additional information on drug interactions and specifically agents that affect QT interval can be found on the following web site: https://crediblemeds.org/.

Drugs that are generally accepted to prolong the QT interval and have an increased risk of torsades de pointes

Alfuzosin, amiodarone, amisulpride, anagrelide, apomorphinete, arformoterol, aripiprazole, arsenictrioxide, asenapine, astemizole, azithromycin, bedaquiline, buserelin, cesium chloride, chloral hydrate, chloroquine, chlorpromazine, ciprofloxacin, cisapride, citalopram, clarithromycin, clozapine, cocaine, crizotinib, dasatinib, disopyramide, dofetilide, dolasetron, domperidone, dronedarone, droperidol, eribulin, erythromycin, flecainide, fluoxetine, formoterol, gatifloxacin, goserelin, granisetron, halofantrine, haloperidol, histrelin, hydroxyzine, hydroxyzine, ibutilide, iloperidone, ivabradine, lapatinib, leuprolide, levofloxacin, lopinavir, loxapine, mefloquine, methadone, metoclopramide, metronidazole, mifepristone, moxifloxacin, nelfinavir, nilotinib, ofloxacin, olanzapine, ondansetron, oxycodone, papaverine, pasireotide, pentamidine, perphenazine, pimozide, pipamperone, posaconazole, probucol, procainamide, propafenone, quetiapine, quinidine, quinine, ranolazine, risperidone, saquinavir, sertindole, sorafenib, sotalol, sparfloxacin, sunitinib, telavancin, telithromycin, terlipressin, thioridazine, thiothixene, toremifene, trazodone, tricyclic and tetracyclic antidepressants, triptorelin, vandetanib, vemurafenib, voriconazole, vorinostat, ziprasidone

Drugs that prolong the PR interval

Acetylcholinesterase inhibitors (donepezil, rivastigmine, galantamine), adenosine, alendronate, antiarrhythmics (flecainide, propafenone, procainamide), beta-blockers, calcium channel blockers, digoxin, dolasetron, lithium, HIV protease inhibitors, lacosamide, methyldopa, pregabalin, TCAs, vitamin D and derivatives

Drugs that shorten the PR interval

Atropine, ibutilide

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Preface K: Drugs Affected by Gastric pH

Drugs with pH-dependent absorption

Drugs that alter gastric pH may alter absorption of drugs with pH-dependent absorption. If concurrent use is required, separate administration of drugs with pH-dependent absorption from antacids by 2 hours, H2 antagonists by 12 hours and avoid PPIs.

ACE inhibitors, allopurinol, ascorbic acid, atazanavir, bisacodyl, bisphosphonates, calcitriol, calcium, cefuroxime, chloroquine, citric acid, corticosteroids, dabigatran, dasatinib, deferasirox, deferiprone, delavirdine, eltrombopag, elvitegravir, erlotinib, ethambutol, fexofenadine, gabapentin, iron, isoniazid, itraconazole, ketoconazole, levothyroxine, mesalamine, misoprostol, multivitamins, mycophenolate, nilotinib, phosphorous, ponatinib, quinine, quinolone antibiotics, sodium polystyrene, strontium, tetracyclines, thyroid products, vitamin D and analogues, vismodegib

Drugs that alter gastric pH

Antacids, H_2 antagonists (cimetidine, ranitidine, famotidine, nizatidine), proton pump inhibitors (dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole)

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Preface L: Abbreviations

These are the abbreviations used commonly through these flash cards:

ACE	Angiotensin-converting enzyme
ACE-I	Angiotensin-converting enzyme inhibitor
AChE	Acetylcholinesterase
ADHD	Attention-deficit hyperactivity disorder
ADP	Adenosine diphosphate
AEDs	Antiepileptic drugs
ALT	Alanine transaminase
AMI	Acute myocardial infarction
AMP	Adenosine monophosphate
AMPA	α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
aPTT	Activated partial thromboplastin time
ARB	Angiotensin II receptor blocker
AST	Aspartate transaminase
ATP	Adenosine triphosphate
AUA	American Urologic Association
AUC	Area under the (time-concentration) curve
AV	Atrioventricular
AVP	Arginine vasopressin
B. fragilis	*Bacteroides fragilis*
bid	Twice daily (*bis in die*)
BMD	Bone mineral density
BP	Blood pressure
BPH	Benign prostatic hyperplasia
BUN	Blood urea nitrogen
C. difficile	*Clostridium difficile*
C. parvum	*Cryptosporidium parvum*
C. trachomatis	*Chlamydia trachomatis*
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CBC	Complete blood count
CCR5	C-C motif receptor 5
CK	Creatine kinase
CKD	Chronic kidney disease
Cmax	Concentration, maximum (on time-concentration curve)
CNS	Central nervous system
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
COPD	Chronic obstructive pulmonary disease
CR	Controlled release
CrCl	Creatinine clearance
CSF	Cerebrospinal fluid
CV	Cerebrovascular
CYP	Cytochrome P
d	Day
DEXA	Dual-energy x-ray absorptiometry
DHA	Docosahexaenoic acid
DHFR	Dihydrofolate reductase
DILE	Drug-induced lupus erythematosus

dL	Deciliter
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
DPP-4	Dipeptidyl peptidase-4
DVT	Deep vein thrombosis
DTaP	Diphtheria and tetanus toxoids
E. coli	*Escherichia coli*
E. histolytica	*Entamoeba histolytica*
ECG	Electrocardiogram
EEG	Electroencephalogram
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
EPA	Eicosapentaenoic acid
ER	Extended release
ESR	Erythrocyte sedimentation rate
ESRD	End-stage renal disease
F	Bioavailability
FAA	Federal Aviation Administration
FBG	Fasting blood glucose
FDA	Food and Drug Administration
FPG	Fasting plasma glucose
FSH	Follicle-stimulating hormone
G. lamblia	*Giardia lamblia*
GABA	γ-Aminobutyric acid
GERD	Gastroesophageal reflux disease
GI	Gastrointestinal
GMP	Guanosine monophosphate
G6PD	Glucose-6-phosphate dehydrogenase
h	Hour
H. influenzae	*Haemophilus influenzae*
H. pylori	*Helicobacter pylori*
Hgb	Hemoglobin
HbA_{lc}	Glycosylated hemoglobin (hemoglobin A_{lc})
HBV	Hepatitis B virus
Hct	Hematocrit
HCT	Hydrocortisone
HCTZ	Hydrochlorothiazide
HDL	High-density lipoprotein
HgB	Hemoglobin
HIV	Human immunodeficiency virus
HMG-CoA	Hydroxymethylglutaryl-CoA
HPA	Hypothalamic axis
HPV	Human papillomavirus
HR	Heart rate
hs	At bedtime (*hora somni*)
HSV	Herpes simplex virus
$5\text{-}HT_1$	5-hydroxytryptamine 1
HTN	Hypertension
HZV	Herpes zoster virus
IM	Intramuscular; infectious mononucleosis
INR	International normalized ratio
IOP	Intraocular pressure
ISMN	Isosorbide mononitrate

IUD	Intrauterine device
IV	Intravenous; Roman numeral four; symbol for class 4 controlled substances
LABA	Long-acting beta-agonist
LDL	Low-density lipoprotein
LH	Luteinizing hormone
LFT	Liver function test
M. avium	*Mycobacterium avium*
M. (B.) catarrhalis	*Moraxella (Branhamella) catarrhalis*
MAOI	Monoamine oxidase inhibitor
MCV	Mean corpuscular volume
MDD	Major depressive disorder
MDI	Metered-dose inhaler
mEq	Milliequivalent
mg	Milligram
MHD	Monohydroxy metabolite
MI	Myocardial infarction; mitral insufficiency
min	Minute
MMR	Measles-mumps-rubella
mo	Month
MRI	Magnetic resonance imaging
MRSA	Methicillin-resistant *S. aureus*
N. meningitides	*Neisseria meningitides*
NG	Nasogastric
NMDA	*N*-methyl-d-aspartate
NO	Nitric oxide
NSAID	Nonsteroidal anti-inflammatory drug
NSR	Normal sinus rhythm
NYHA	New York Heart Association
OCD	Obsessive-compulsive disorder
OTC	Over-the-counter
P. aeruginosa	*Pseudomonas aeruginosa*
P. carinii	*Pneumocystis carinii*
P. falciparum	*Plasmodium falciparum*
P. malariae	*Plasmodium malariae*
P. vivax	*Plasmodium vivax*
PBPs	Penicillin-binding proteins
PCP	*Pneumocystis carinii* pneumonia
PDE5	Phosphodiesterase type 5
PDEI	Phosphodiesterase inhibitor
PE	Pulmonary embolism
PEG	Polyethylene glycol
PFOR	Pyruvate ferredoxin oxidoreductase
PFT	Pulmonary function test
PMDD	Premenstrual dysphoric disorder
po	By mouth (*per os*)
PPAR-α	Peroxisome proliferator–activated receptor-α
PPAR-γ	Peroxisome proliferator–activated receptor-γ
PPI	Proton pump inhibitor
pr	Per rectum
PrEP	Preexposure prophylaxis
prn	When necessary, as needed (*pro re nata*)
PSA	Prostate-specific antigen

PTSD	Posttraumatic stress disorder
PUD	Peptic ulcer diseases
qid	Four times daily (*quater in die*)
qod	Every other day
qwk	Every week
REMS	Risk evaluation and mitigation strategy
RNA	Ribonucleic acid
s	Second
S. aureus	*Staphylococcus aureus*
S. pneumoniae	*Streptococcus pneumoniae*
SA	Sino-atrial
SABA	Short-acting beta-agonists
SAD	Seasonal affective disorder
SCr	Serum creatinine
SERM	Selective estrogen receptor modulator
SMZ/TMP	Sulfamethoxazole/trimethoprim
SNRI	Serotonin-norepinephrine reuptake inhibitor
sq	Subcutaneous
SSKI	Saturated solution of potassium iodide
SSRI	Selective serotonin reuptake inhibitor
T. mentagrophytes	*Trichophyton mentagrophytes*
T. rubrum	*Trichophyton rubrum*
T. vaginalis	*Trichomonas vaginalis*
TCA	Tricyclic antidepressant
Tdap	Tetanus and diphtheria toxoid
TG	Triglyceride
TIBC	Total iron-binding capacity
tid	Three times daily (*ter in die*)
Tmax	Time to maximum concentration (on time-concentration curve)
TSH	Thyroid-stimulating hormone
TTP	Thrombotic thrombocytopenic purpura
UGT	Uridine diphosphate glucuronosyltransferase
UTI	Urinary tract infection
Vd	Volume of distribution
VLDL	Very low-density lipoprotein
VZS	Varicella-zoster virus
WBC	White blood cell (count)
wk	Week
XR	Extended release
y	Year

ACYCLOVIR: Zovirax, Various

Class: Viral DNA Polymerase Inhibitor

Dosage Forms. Capsule: 200 mg; **Suspension:** 200 mg/5 mL; **Tablet:** 400 mg, 800 mg

Teva generic 200 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Genital herpes simplex: Adults, initial episode, 400 mg po tid or 200 mg po 5 times a day × 7-10 d; Children ≥12 y of age, 1000-1200 mg/d po in 3-5 divided doses for 7-10 d
2. Genital herpes simplex, suppressive therapy: 400 mg po bid for up to 12 mo
3. Herpes zoster, shingles: 800 mg po 5 times a day × 7-10 d
4. Varicella: Adults and Children ≥2 y of age and ≥40 kg, 800 mg po qid × 5 d; Children ≥2 y of age and <40 kg, 20 mg/kg po qid × 5 d

Off-Label Uses.

1. Genital herpes simplex in HIV-positive patients, initial or recurrent: 400 mg po tid × 5-10 d
2. Genital herpes simplex in HIV-positive patients, chronic suppression: 400-800 mg po bid-tid

MOA. Acyclovir is an acyclic nucleoside analogue of deoxyguanosine that is selectively phosphorylated by the virus-encoded thymidine kinase to its monophosphate form. Cellular enzymes then convert the monophosphate to the active antiviral acyclovir triphosphate, which competitively inhibits viral DNA synthesis by inactivation of viral DNA polymerase and incorporation into and termination of viral DNA replication. Acyclovir has potent activity against herpes simplex virus (HSV) I and II and herpes zoster virus (varicella-zoster virus [VZV]).

Drug Characteristics: Acyclovir

Dose Adjustment Hepatic	Not required	**Absorption**	F = 10-20%, food has no effect on absorption
Dose Adjustment Renal	CrCl 10-25 mL/min, increase interval to q8h; CrCl <10 mL/min, increase interval to q12h	**Distribution**	Vd = 0.8 L/kg; 9-33% protein bound Placenta, CSF, kidney, brain, lung, heart
Dialyzable	Hemodialysis removes 60% of dose. No adjustment for peritoneal (<10% removed)	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 62-90% with a half-life of 2.5-3.3 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to acyclovir or valacyclovir	**Black Box Warnings**	None

Medication Safety Issues: Acyclovir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Acyclovir

Typical Agents	Mechanism	Clinical Management
Phenytoin, fosphenytoin, valproic acid	Decreased absorption and lower plasma concentration of phenytoin	Monitor phenytoin levels and adjust, if necessary
Varicella virus vaccine	Decreased vaccine effectiveness via antagonism	Avoid concurrent use

Adverse Reactions: Acyclovir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Malaise	Nausea, vomiting, headache, diarrhea	Severe hypersensitivity, renal failure, TTP

Efficacy Monitoring Parameters. Resolution of clinical signs of infection (lesions) within 2-3 d.

Toxicity Monitoring Parameters. Seek medical attention if decreased urination, unusual bruising or bleeding, blistering skin rash, shortness of breath, confusion, lethargy, or seizures.

Key Patient Counseling Points. Complete full course of therapy. Ensure adequate hydration. For HSV, initiate treatment as soon as possible at first sign of lesion. For VZV, treatment should begin within 24 h of appearance of rash. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If using for prophylaxis, this medication should reduce the number of breakouts.

Clinical Pearls. Not indicated for children <2 y of age. Use caution with concurrent nephrotoxins. Topical and parenteral products also available.

ADAPALENE: Differin, Various

Class: Retinoid, Antiacne

Dosage Forms. Cream: 0.1%; **Gel/Jelly:** 0.1%, 0.3%; **Lotion:** 0.1%

Common FDA Label Indication, Dosing, and Titration.

1. Acne vulgaris: Adults and Children >12 y of age, apply thin film topically to affected area(s) daily hs

Galderma 0.3% gel pictured

Off-Label Uses. None

MOA. Adapalene exhibits retinoic acid-like activity, reducing important features of the pathology of acne vulgaris by normalizing the differentiation of follicular epithelial cells and keratinization to prevent microcomedone formation. Adapalene enhances keratinocyte differentiation without inducing epidermal hyperplasia and severe irritation, which is associated with retinoic acid. Adapalene decreases formation of comedones, and inflammatory and noninflammatory acne lesions.

Drug Characteristics: Adapalene

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not applicable
Dialyzable	Unknown	**Metabolism**	Not applicable
Pregnancy Category	C	**Elimination**	Not applicable
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Adapalene

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Adapalene

Typical Agents	Mechanism	Clinical Management
Oral contraceptives	Decreased serum concentration of progestin	Consider 2 forms of contraception, particularly if patient is taking progesterone-only preparation

Adverse Reactions: Adapalene

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dry skin, scaly skin, erythema, burning/stinging	Skin irritation, skin discomfort, pruritus	Angioedema

Efficacy Monitoring Parameters. Improvement in acne.

Toxicity Monitoring Parameters. Severe dry skin or severe skin irritation.

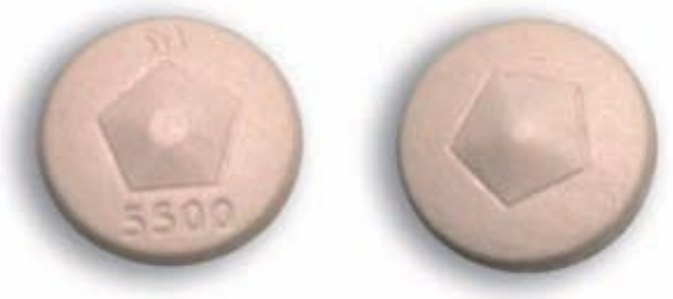
Key Patient Counseling Points. Avoid contact with eyes, lips, angles of nose, and mucous membranes; do not apply on cuts, abrasions, eczematous, or sunburned skin. Wash, then dry hands and affected area prior to application. Use of moisturizers may be necessary for relief of dry skin or irritation. Avoid products that can dry or irritate skin further. If cutaneous reactions (such as erythema, scaling, and stinging/burning) are severe, the frequency should be reduced or adapalene discontinued. Other topical preparations (sulfur, resorcinol, or salicylic acid) should not be used prior to using topical adapalene. Adapalene causes sun sensitivity. Avoid sun exposure and tanning beds. Protective clothing and application of sunscreen are recommended when sun exposure cannot be avoided. Cold temperatures or wind may also increase skin irritation during drug therapy. Symptomatic improvement may not be seen for a few months.

Clinical Pearls. Safety and efficacy have not been established in children <12 y of age.

ALBENDAZOLE: Albenza

Class: Anthelmintic

Dosage Forms. Tablet: 200 mg



GlaxoSmithKline 200 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Parenchymal neurocysticercosis caused by *Taenia solium*: Adults ≥60 kg, 400 mg po bid with meals × 8-30 d; Children <60 kg, 15 mg/kg/d (*max* 800 mg/d) in 2 divided doses × 8-30 d
2. Cystic hydatid disease of the liver, lung, and peritoneum caused by *Echinococcus granulosus*: Adults ≥60 kg, 400 mg po bid with meals × 8-30 d; Children <60 kg, 15 mg/kg/d (*max* 800 mg/d) in 2 divided doses × 8-30 d

Off-Label Uses.

1. *Ancylostoma caninum, Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (hookworm), and *Necator americanus* (hookworm): 400 mg po as a single dose
2. *Enterobius vermicularis* (pinworm): 400 mg po as a single dose, repeat in 2 wk
3. *Giardia duodenalis* (giardiasis): 400 mg po once daily × 5 d

MOA. Selective degeneration of cytoplasmic microtubules in intestinal and tegmental cells of intestinal helminths and larvae. This leads to impaired glucose uptake in parasites and ATP production decreases leading to energy depletion and death.

Drug Characteristics: Albendazole

Dose Adjustment Hepatic	Caution with hepatic dysfunction	**Absorption**	F <5%, food enhances absorption up to 5 times
Dose Adjustment Renal	Not required	**Distribution**	Cyst, CSF
Dialyzable	Not dialyzable	**Metabolism**	Hepatic to 1 active metabolite; minor substrate of CYP3A4/5, 1A2
Pregnancy Category	C	**Elimination**	<1% renal with half-life of 8-15 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to albendazole	**Black Box Warnings**	None

Medication Safety Issues: Albendazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Aplenzin, Relenza	No

Drug Interactions: Albendazole

Typical Agents	Mechanism	Clinical Management
Grapefruit juice	Increased oral availability of albendazole	Often administered together to enhance absorption

Adverse Reactions: Albendazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headaches, elevated LFTs	Nausea, vomiting, abdominal pain, dizziness, diarrhea, alopecia	Severe hypersensitivity, renal failure, hepatic failure, aplastic anemia, agranulocytosis, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Monitor fecal specimens for ova and parasites for 3 wk after treatment; if positive, retreat. Ophthalmic examination in those with neurocysticercosis.

Toxicity Monitoring Parameters. LFTs and CBC at beginning of each 28-d cycle and every 2 wk. Negative pregnancy test prior to starting therapy.

Key Patient Counseling Points. Complete full course of therapy; administer with high-fat meals or grapefruit juice. Avoid pregnancy for at least 1 mo post-treatment. In children or those with difficulty swallowing tablets, tablets can be crushed or chewed and swallowed with water.

Clinical Pearls. Single-dose therapy makes this agent a treatment of choice for nematode infections. Neurocysticercosis: Use concurrent corticosteroids to minimize inflammatory reactions and anticonvulsant therapy to prevent seizures. Echinococcosis: More effective than mebendazole, so may be treatment of choice.

ALBUTEROL: ProAir HFA, Proventil HFA, Ventolin HFA, Various

A

Class: Selective β_2-Adrenergic Agonist

Dosage Forms. **Metered-Dose Inhaler (MDI):** 90 (base) mcg/actuation; **Tablet:** 2 mg, 4 mg; **Extended-Release Tablet:** 4 mg, 8 mg; **Syrup:** 2 mg/5 mL; **Inhalation Solution:** 0.021%, 0.042%, 0.083%

Common FDA Label Indication, Dosing, and Titration.

1. Asthma (acute exacerbation): Adults, MDI, 4-8 inhalations every 20 min up to 4 h, then every 1-4 h prn; Children, 4-8 inhalations every 20 min for 3 doses, then every 1-4 h prn (use mask for children <4 y of age)
2. Asthma (bronchospasm): Adults and Children, MDI, 2 inhalations every 4-6 h prn; Adults and Children ≥12 y of age, oral, 2-4 mg immediate-release tablet po tid or qid or 4-8 mg extended-release tablet po q12h (*max* of 32 mg/d); Children 6-11 y of age, 2 mg immediate-release tablet po tid or qid or 4 mg extended-release tablet po q12h; Children 2-6 y of age, 0.1 mg/kg oral syrup po tid
3. Exercise-induced asthma, prevention: Adults, 2 inhalations 15-30 min prior to exercise; Children ≥4 y of age, 2 inhalations 15-30 min prior to exercise

ProAir HFA by Teva pictured

Off-Label Uses.

COPD: 2 inhalations every 4-6 h prn

MOA. Albuterol is a selective β_2-adrenergic agonist that acts on β_2-adrenergic receptors of intracellular adenyl cyclase to increase cyclic AMP levels resulting in bronchial smooth muscle relaxation.

Drug Characteristics: Albuterol

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50-85% (oral tablet), 100% (extended-release tablet), food decreases rate (but not extent) of absorption of extended-release tablet
Dose Adjustment Renal	Not required	**Distribution**	Vd = 156 L; 10% protein bound
Dialyzable	Unknown	**Metabolism**	20% via sulfotransferases
Pregnancy Category	C	**Elimination**	80% renal elimination, half-life (inhalation) 3.8 h, (oral) 3.7-5 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Albuterol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush extended-release tablets	No	Albutein, atenolol, Prilosec, Prinivil, Vantin	No

Drug Interactions: Albuterol

Typical Agents	Mechanism	Clinical Management
Other short-acting sympathomimetics	May potentiate albuterol effect and increase risk of cardiovascular adverse effects	Avoid concurrent use
Beta-blockers (nonselective)	May decrease effectiveness of albuterol and produce bronchospasms	Avoid nonselective beta-blockers; monitor PFT if cardioselective beta-blockers used
Diuretics (non-potassium sparing)	May potentiate hypokalemia	Monitor potassium levels
Digoxin	May decrease digoxin levels	Monitor digoxin levels
MAOI and tricyclic antidepressants	May potentiate albuterol effect on cardiovascular system	Consider alternative therapy

Adverse Reactions: Albuterol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, pharyngitis, rhinitis, throat irritation, upper respiratory tract infections	Angina, tachycardia, hypokalemia, tremor, nervousness, insomnia, cough, headache, viral lower respiratory infection	Paradoxical bronchospasms, pulmonary edema, atrial fibrillation

Efficacy Monitoring Parameters. Resolution of asthma symptoms and PFTs.

Toxicity Monitoring Parameters. Use alternative therapy or seek emergency treatment if paradoxical bronchospasm occurs.

Key Patient Counseling Points. Instruct patient on inhaler technique, including priming and shaking well before using. Wash the mouthpiece and air dry thoroughly at least once a week (may cease to deliver medication if mouthpiece becomes blocked). Part of the extended-release tablet may pass into stool. Contact prescriber if more albuterol is needed to control symptoms than usual as this may indicate asthma deterioration. Report need to increase frequency of use for symptomatic relief to physician. Do not use more frequently than recommended.

Clinical Pearls. The National Heart, Lung, and Blood Institute asthma guidelines recommend short-acting beta-agonists (SABA) as the drug of choice for treating acute asthma symptoms and exacerbations. Do not use SABA as a component of chronic therapy without an anti-inflammatory agent. Solution for nebulization also available. MDI can be used with spacer if need be for proper administration. Some MDIs have a dose counter to help patient keep track of doses.

ALENDRONATE: Fosamax, Binosto, Various

Class: Bisphosphonate

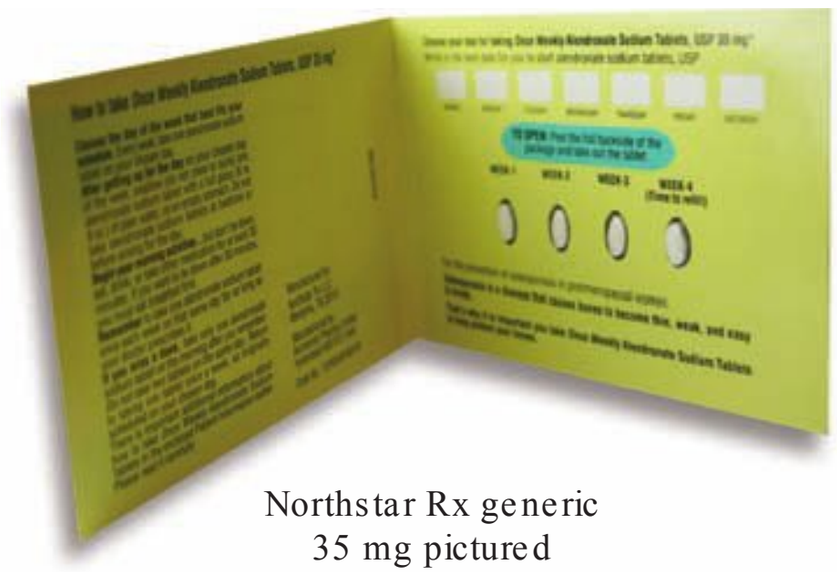
Dosage Forms. Tablet: 5 mg, 10 mg, 35 mg, 40 mg, 70 mg; **Solution:** 70 mg/75 mL; **Effervescent Tablet:** 70 mg

Common FDA Label Indication, Dosing, and Titration.

1. Postmenopausal osteoporosis: 70 mg po once weekly or 10 mg po daily
2. Postmenopausal osteoporosis, prophylaxis: 5 mg po daily or 35 mg po once weekly
3. Paget disease: 40 mg po daily for 6 mo
4. Osteoporosis, male: 10 mg once daily or 70 mg once weekly
5. Glucocorticoid-induced osteoporosis in those with daily dosage ≥7.5 mg of prednisone (or equivalent): 5 mg once daily; a dose of 10 mg once daily should be used in postmenopausal females who are not receiving estrogen

Off-Label Uses.

1. Postoperative knee arthroplasty: 10 mg once daily beginning after knee arthroplasty for up to 1 y



Northstar Rx generic
35 mg pictured

MOA. Alendronate binds to bone hydroxyapatite, and at the cellular level, inhibits osteoclast activity, thereby inhibiting bone resorption and modulating bone metabolism.

Drug Characteristics: Alendronate

Dose Adjustment Hepatic	Not required	**Absorption**	F <1%, food impairs absorption, take 30-60 min prior to meal
Dose Adjustment Renal	CrCl <35 mL/min: avoid use	**Distribution**	Vd = 2576 L; 78% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 50% with a half-life in bone of more than 10 y
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Esophageal abnormalities, hypersensitivity, hypocalcemia, inability to sit or stand upright for at least 30 min; increased risk for adverse esophageal effects	**Black Box Warnings**	None

Medication Safety Issues: Alendronate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Fosamax Plus D	No	No	No	Risedronate, Flomax, Zithromax, fosinopril	No

Drug Interactions: Alendronate

Typical Agents	Mechanism	Clinical Management
Aluminum, calcium, magnesium, or iron-containing products	Decreased bisphosphonate absorption	Separate administration by at least 30 min after alendronate, ideally 1-2 h

Adverse Reactions: Alendronate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Fever, flu-like syndrome, gastric ulcer	Myalgia, bone pain, esophageal ulcer, abdominal pain, constipation, diarrhea, flatulence, indigestion, headache	Osteonecrosis of the jaw, esophageal cancer, immune hypersensitivity, arrhythmia, fractures

Efficacy Monitoring Parameters. Increased BMD (T-score), decreased incidence of bone fractures.

Toxicity Monitoring Parameters. Baseline serum creatinine, calcium, phosphorous, severe skin rash, difficulty swallowing, swelling, tooth problems, severe pain.

Key Patient Counseling Points. Swallow the noneffervescent tablet whole with a large glass (240 mL) of plain water only. Dissolve 1 effervescent tablet in 120 mL of room temperature plain water only (not mineral water or flavored water); once effervescence stops, wait ≥5 min and stir the solution for ~10 s and then drink. Wait at least 30 min after you swallow the tablet before you eat or drink anything or take any other medicines. This will help your body absorb the medicine. Do not lie down for at least 30 min after taking this medicine, and do not lie down until after you have eaten some food.

Clinical Pearls. Concurrent chemotherapy and poor oral hygiene increase the risk of osteonecrosis of the jaw. Atypical fractures of the thigh have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Adequate calcium and vitamin intake required for efficacy. Men >70 y of age and women >50 y of age should consume 1200 mg of elemental calcium from all sources (dietary + supplements) and all adults >50 y of age should consume 800-1000 units of vitamin D daily with a target serum level of >30 ng/mL.

ALLOPURINOL: Zyloprim, Various

A

Class: Xanthine Oxidase Inhibitor; Antigout

Dosage Forms. Tablet: 100 mg, 300 mg

Northstar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Gout, mild: 100-300 mg po daily; *max* dose 800 mg/d
2. Gout, moderate to severe: 400-600 mg po daily in 2-3 divided doses, *max* dose 800 mg/d
3. Hyperuricemia, tumor lysis syndrome: Children <6 y, 50 mg po tid or 150 mg po daily for 2-3 d; Children 6-10 y, 100 mg po tid or 300 mg po daily for 2-3 d; Adults, 600-800 mg/d po daily in 2-3 divided doses for 2-3 d; starting 12 h-3 d prior to chemotherapy

Off-Label Uses.

1. Malaria: 12 mg/kg/d po in 3 divided doses × 5 d, with quinine

MOA. Allopurinol decreases the production of uric acid by inhibiting the action of xanthine oxidase, the enzyme that converts hypoxanthine to xanthine and xanthine to uric acid.

Drug Characteristics: Allopurinol

Dose Adjustment Hepatic	Not required	**Absorption**	F = 80-90%, no effect of food on absorption
Dose Adjustment Renal	CrCl 10-20 mL/min, 200 mg po daily; CrCl 3-9 mL/min, 100 mg po daily, CrCl <3 mL/min, 100 mg at extended intervals (>24 h)	**Distribution**	Vd = 1.6-2.43 L/kg; <1% protein bound
Dialyzable	Yes, supplementation may be needed after dialysis	**Metabolism**	Metabolized in the liver (78%) and red blood cells
Pregnancy Category	C	**Elimination**	Renal elimination is 80% with a half-life of 2 h, active metabolite (oxypurinol) has half-life of 15-25 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to allopurinol, concurrent use of didanosine	**Black Box Warnings**	None

Medication Safety Issues: Allopurinol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zovirax, Apresoline	No

Drug Interactions: Allopurinol

Typical Agents	Mechanism	Clinical Management
Didanosine	Increased didanosine bioavailability	Avoid concurrent use
Azathioprine	Xanthine oxidase needed to eliminate azathioprine metabolite, mercaptopurine; when xanthine oxidase is inhibited by allopurinol, increases azathioprine effect and toxicity	Reduce azathioprine dose by 1/3 or avoid concurrent use
Cyclophosphamide	Unknown; increased cyclophosphamide toxicity (bone marrow suppression)	Avoid concurrent use

Adverse Reactions: Allopurinol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Rash, maculopapular eruption, acute attacks of gout with initiation	Stevens-Johnson syndrome, toxic epidermal necrolysis, agranulocytosis, aplastic anemia, thrombocytopenia, granulomatous hepatitis, hepatotoxicity, immune hypersensitivity reaction, renal failure

Efficacy Monitoring Parameters. Resolution of clinical signs of gout (pain, stiffness), serum uric acid concentrations measured after 48 h of therapy.

Toxicity Monitoring Parameters. LFTs, renal function, CBC.

Key Patient Counseling Points. Take after meals to lessen gastric irritation. Maintain adequate hydration during therapy to prevent kidney stones. Patient should avoid alcohol or caffeine while taking allopurinol. Seek medical attention if signs and symptoms of myelosuppression, agranulocytosis (severe neutropenia), or Stevens-Johnson syndrome (flu-like symptoms, spreading red rash, or skin/mucous membrane blistering) occur.

Clinical Pearls. Allopurinol for injection is also available, and has been designated an orphan product for use in the treatment of elevated serum or urinary uric acid levels secondary to lymphomas, leukemias, or solid tumors in patients intolerant of oral therapy. Full effect of allopurinol in chronic gout may take 2-6 wk, slow dose titration recommended.

ALPRAZOLAM: Xanax, Various

Class: Benzodiazepine, Short or Intermediate. C-IV

Dosage Forms. Tablet: 0.25 mg, 0.5 mg, 1 mg, 2 mg; **Tablet, Disintegrating:** 0.25 mg, 0.5 mg, 1 mg, 2 mg; **Tablet, Extended Release:** 0.5 mg, 1 mg, 2 mg, 3 mg; **Solution:** 1 mg/mL

Sandoz generic
1 mg pictured

Sandoz generic
2 mg pictured

Dava generic
0.5 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Anxiety: immediate-release or orally disintegrating tablet, 0.25-0.5 mg po tid; *max* daily dose, 4 mg in divided doses
2. Panic disorder, with or without agoraphobia: immediate-release or orally disintegrating tablets, 0.5 mg po tid, extended-release 3-6 mg po daily; dose may be increased every 3-4 d by <1 mg/d

Off-Label Uses.

1. Alcohol withdrawal syndrome: 0.5-1 mg po bid × 7-10 d

MOA. Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

Drug Characteristics: Alprazolam

Dose Adjustment Hepatic	Reduce initial dose to 0.25 mg in advanced liver disease	**Absorption**	F = 80%, no effect of food on absorption of immediate release, food increases absorption of ER by 25%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.9-1.2 L/kg, 80% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, 20-30%; major substrate of CYP3A4/5
Pregnancy Category	D	**Elimination**	Renal 80% with a half-life of 10-12 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to benzodiazepines, narrow-angle glaucoma, concurrent ketoconazole, or itraconazole	**Black Box Warnings**	None

Medication Safety Issues: Alprazolam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	ALPRAZolam	ALPRAZolam ER	No	Zantac, LORazepam, Xopenex	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium

Drug Interactions: Alprazolam

Typical Agents	Mechanism	Clinical Management
Alfentanil, opioids, and other respiratory depressants	Additive respiratory depression	Avoid if possible and consider dose reductions of both agents
CYP3A4/5 inducers	Increased alprazolam metabolism reduces alprazolam effectiveness	Monitor and consider dose increases of alprazolam
CYP3A4/5 inhibitors	Decreased alprazolam metabolism increases risk of alprazolam toxicity	Monitor and consider dose decreases of alprazolam
Digoxin	Reduced renal clearance of digoxin and increased digoxin toxicity	Monitor digoxin levels and consider dose reductions
Ethinyl estradiol and other estrogen-based birth control products	Inhibition of alprazolam metabolism and additional toxicity	Use with caution

Adverse Reactions: Alprazolam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Ataxia, lethargy, retrograde amnesia, somnolence, weight gain, change in appetite, constipation, fatigue, cognitive dysfunction, decreased libido	Tachycardia, palpitations, nausea and vomiting, blurred vision, confusion	Seizures, mania, depression, liver failure, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Reduction in anxiety symptoms.

Toxicity Monitoring Parameters. Seek medical attention if severe drowsiness, slow or rapid heartbeat or skipped beats, thoughts of suicide.

Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Do not crush or break extended-release product. Oral disintegrating tablet may be divided, but are unstable after breaking. If only 1/2 tablet taken, discard the other half. Allow oral disintegrating tablet to dissolve on your tongue. Avoid alcohol. Do not self-increase or abruptly discontinue use.

Clinical Pearls. Not for use in children. Consider reduced dose of benzodiazepines in hepatic impairment. Avoid use in elderly, appear more sensitive to the effects. Use CNS depressants concurrently with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. In general, should only be used for short periods of time, reevaluate need frequently.

AMITRIPTYLINE: Elavil, Various

Sandoz generic pictured

Class: Tricyclic Antidepressant

Dosage Forms. Tablet: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Adults, 75 mg po divided into 1-3 daily doses, titrate to *max* 300 mg/d; Children ≥12 y of age, 10 mg po tid or 20 mg po daily hs

Off-Label Uses.

1. Migraine prophylaxis: 10-25 mg po daily hs; titrate to *max* 150 mg/d
2. Chronic pain: 25-100 mg po daily hs; titrate to *max* 150 mg/d
3. Polyneuropathy, postherpetic neuralgia, treatment and prophylaxis: 10-25 mg po daily hs; may titrate to *max* 200 mg/d
4. Post-traumatic stress disorder (PTSD): 50 mg po daily; titrate to *max* 300 mg/d

MOA. Amitriptyline is a tricyclic antidepressant that blocks presynaptic reuptake of serotonin and norepinephrine with subsequent down-regulation of adrenergic receptors.

Drug Characteristics: Amitriptyline

Dose Adjustment Hepatic	Start with low initial doses and increase as needed and tolerated	**Absorption**	F = 100%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd is highly variable
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; minor substrate of CYP1A2, 2B6, 2C9, 2C19, and 3A4/5; major substrate of CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is minimal with a half-life of 9-27 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity; concurrent MAOI or MAOI use in last 14 d; use during acute recovery period after MI	**Black Box Warnings**	Suicidality; not approved for children <12 y of age

Medication Safety Issues: Amitriptyline

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Enalapril, imipramine, nortriptyline	Avoid. Highly anticholinergic, sedating, and cause orthostatic hypotension

Drug Interactions: Amitriptyline

Typical Agents	Mechanism	Clinical Management
Anticholinergics	Additive adverse effects	Avoid concurrent use or monitor carefully
Antiarrhythmics, and drugs that cause QT prolongation	Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest)	Avoid concurrent use
CYP2D6 inducers	Increased amitriptyline metabolism reduces amitriptyline effectiveness	Monitor and consider dose increases of amitriptyline
CYP2D6 inhibitors	Decreased amitriptyline metabolism increases risk of amitriptyline toxicity	Monitor and consider dose decreases of amitriptyline
Linezolid, MAOIs, methylene blue, SSRIs	Increased risk of serotonin syndrome	Concomitant use with MAOIs contraindicated, others with caution

Adverse Reactions: Amitriptyline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Sedation	Blurred vision, confusion, constipation, dizziness, sexual dysfunction, somnolence, urinary retention, weight gain, xerostomia	Cardiac dysrhythmia, hepatotoxicity, seizures, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in target symptoms of depression. Reduction or improvement in pain or decreased frequency of migraines.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Monitor ECGs and LFTs.

Key Patient Counseling Points. Avoid activities requiring mental alertness, alcohol, and other CNS depressants. Symptomatic improvement may not be seen for a few weeks. Avoid sudden discontinuation of drug. Do not use alcohol.

Clinical Pearls. Safety and effectiveness in children <12 y of age have not been established. Antidepressants increased the risk of suicidal thinking and behavior in children, adolescents, and young adults in short-term studies with major depressive disorder (MDD) and other psychiatric disorders. This drug can cause anticholinergic side effects.

AMLODIPINE: Norvasc, Various

Class: Calcium Channel Blocker

Dosage Forms. Tablet: 2.5 mg, 5 mg, 10 mg

Zygenerics generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Children 6-17 y of age , 2.5-5 mg po daily; Adults, 5-10 mg po daily
2. Stable angina: 5-10 mg po daily
3. Variant angina: 5-10 mg po daily

Off-Label Uses.

1. Diabetic nephropathy: 5-15 mg po daily
2. Left ventricular hypertrophy: 5-10 mg po daily
3. Raynaud phenomenon: 10 mg po daily

MOA. Amlodipine is a long-acting dihydropyridine calcium-channel-blocking drug with potent arterial and coronary vasodilating properties.

Drug Characteristics: Amlodipine

Dose Adjustment Hepatic	Reduce initial dose to 2.5 mg po daily in hepatic impairment	**Absorption**	F = 64-90%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 21 L/kg; 93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, 90%; major substrate of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 10% with a half-life of 30-50 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to amlodipine	**Black Box Warnings**	None

Medication Safety Issues: Amlodipine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	AmLODIPine	No	No	aMILoride Navane, Norvir, Vascor	No

Drug Interactions: Amlodipine

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Increased risk of hypotension, bradycardia	Avoid concurrent use or monitor BP and HR
Clopidogrel	Decreased antiplatelet activity of clopidogrel by amlodipine	Avoid concurrent use
CYP3A4/5 inducers	Increased amlodipine metabolism reduces amlodipine effectiveness	Monitor and consider dose increases of amlodipine
CYP3A4/5 inhibitors	Decreased amlodipine metabolism increases risk of amlodipine toxicity	Monitor and consider dose decreases of amlodipine
NSAIDs	Decreased antihypertensive effect of amlodipine	Avoid concurrent use or monitor BP

Adverse Reactions: Amlodipine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Peripheral edema, pulmonary edema	Abdominal pain, arthralgia, constipation, dizziness, fatigue, f ushing, headache, hypotension, hyperkalemia, impotence, myalgia, nausea, palpitations, pruritus, rash, tachycardia, urticaria	Hepatotoxicity, thrombocytopenia, AMI, angina

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema, increased HR, LFTs.

Key Patient Counseling Points. Instruct patient to report signs/symptoms of hypotension or exacerbation of angina with initial dosing and dose changes. Avoid alcohol while taking drug. Report signs/symptoms of peripheral edema, fatigue, hypotension, or hepatic dysfunction. Do not discontinue drug suddenly as this may cause rebound hypertension. This medicine may cause dizziness. Avoid activities that could be dangerous if not alert. Dizziness may be worse if too much water is lost from the body due to excessive sweating, diarrhea, or vomiting.

Clinical Pearls. Safety and efficacy not established in pediatric patients <6 y of age. Elderly, small, or frail patients, or when adding to other antihypertensive therapy, decrease initial dose by 2.5 mg po daily.

AMOXICILLIN: Amoxil, Various

Class: β-Lactam Antibiotic

Dosage Forms. Capsule: 250 mg, 500 mg; **Chewable Tablet:** 125 mg, 200 mg, 250 mg, 400 mg; **Drop:** 50 mg/mL; **Suspension:** 125 mg/5 mL, 200 mg/5 mL; 250 mg/5 mL, 400 mg/5 mL; **Tablet:** 500 mg, 875 mg; **Tablet, Extended Release:** 775 mg

Sandoz generic 250 mg pictured

Teva generic 250 mg pictured

Aurobindo generic 875 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute otitis media: Adults, 500-875 mg po q12h × 10 d; Children, 80-90 mg/kg/d po in 2-3 divided doses
2. Lower respiratory tract infection: Adults, 1 g po tid × 10 d; Children, 45 mg/kg/d divided q12h
3. Pharyngitis, tonsillitis: Adults and Children >12 y, 775 mg po daily × 10 d
4. Streptococcal pharyngitis: Adults, 1 g po daily × 10 d; Children, 50 mg/kg po once daily for 10 d, *max* 1 g daily
5. Ear, nose, and throat infection, infection of skin and/or subcutaneous tissue, infection of genitourinary system: Adults, 500-875 mg po q12h × 10 d; Children, 25-45 mg/kg/d po divided q12h
6. *Helicobacter pylori* gastrointestinal tract infection: 1 g po bid with PPI

Off-Label Uses.

1. Bacterial endocarditis, prophylaxis: Adults, 2 g po 1 h before procedure; Children, 50 mg/kg po 1 h prior to procedure, *max* 2 g daily
2. Lyme disease: 500 mg po tid × 21-30 d; Children: 50 mg/kg/d po in 3 divided doses × 21-30 d

MOA. Semisynthetic penicillin derivative that inhibits the biosynthesis of bacterial cell wall mucopeptide. Typically active against *Streptococcus*, *Enterococcus, Staphylococcus*, and Enterobacteriaceae.

Drug Characteristics: Amoxicillin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 85%, no effect of food on absorption
Dose Adjustment Renal	Moderate, increase interval to 8-12 h; severe, increase interval to q24h	**Distribution**	17-20% protein bound. Lung, pleural f uid, bile, liver, and inner ear
Dialyzable	Yes (hemodialysis only)	**Metabolism**	Partially hepatic
Pregnancy Category	B	**Elimination**	Renal elimination is 50-70% with a half-life of 1-2 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Amoxicillin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Extended-release tablet	No	Amoxapine, Augmentin	No

Drug Interactions: Amoxicillin

Typical Agents	Mechanism	Clinical Management
Methotrexate	Decreased methotrexate clearance	Avoid concurrent use or consider methotrexate dose reduction or monitoring levels
Venlafaxine	Increased risk of serotonin syndrome	Avoid concurrent use
Warfarin	Increased risk of bleeding	Increase warfarin monitoring

Adverse Reactions: Amoxicillin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea	Skin rash, vomiting, headache	Severe hypersensitivity, renal failure, hepatic failure, pancytopenia

Efficacy Monitoring Parameters. Resolution of clinical signs of infection.

Toxicity Monitoring Parameters. Severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

Key Patient Counseling Points. Complete full course of therapy and take exactly as directed. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Can take with food if causes upset stomach. Avoid mixing suspension with food or beverages and use with measuring device that comes with prescription. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

Clinical Pearls. There is cross-hypersensitivity between penicillin and cephalosporins; use with caution in cephalosporin allergic. May resume normal activities after 24 h of antibiotics if afebrile. Extended-release tablet not approved for children <12 y of age. Combination with clavulanate preferred for acute bacterial rhinosinusitis. May decrease effectiveness of oral contraceptives.

AMOXICILLIN/CLAVULANATE: Augmentin, Various

Class: β-Lactam Antibiotic

875 mg/125 mg 500 mg/125 mg

Teva generic pictured

Dosage Forms. Tablet: 250 mg amoxicillin/125 mg clavulanate, 500 mg amoxicillin/125 mg clavulanate; 875 mg amoxicillin/125 mg clavulanate; **Tablet, Extended Release:** 1000 mg amoxicillin/62.5 mg clavulanate; **Chewable Tablet:** 200 mg amoxicillin/28.5 mg clavulanate, 400 mg amoxicillin/57 mg clavulanate; **Suspension:** 125 mg amoxicillin/31.25 mg clavulanate/5 mL, 200 mg amoxicillin/28.5 mg clavulanate/5 mL, 250 mg amoxicillin/62.5 mg clavulanate/5 mL; 400 mg amoxicillin/57 mg clavulanate/5 mL, 600 mg amoxicillin/42.9 mg clavulanate/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Acute otitis media: Adults, 500-875 mg po q12h × 10 d; Children, 80-90 mg/kg/d po in 2-3 divided doses
2. Community acquired pneumonia: Adults, 2000 mg po bid × 7-10 d
3. Lower respiratory tract infection: Adults, 1000 mg po tid × 10 d; Children, 45 mg/kg/d po divided q12h
4. Sinusitis, infection of skin or subcutaneous tissue, infectious disease of genitourinary system: Adults, 500-875 mg po q12h × 10 d; Children, 25-45 mg/kg/d po divided q12h

Other Uses.

1. Streptococcal pharyngitis: Adults, 875 mg po q12h or 500 mg po q8h; Children, 45 mg/kg/d divided q12h

MOA. Amoxicillin is a semisynthetic penicillin derivative. Typically active against *Streptococcus, Enterococcus, Staphylococcus*, and Enterobacteriaceae. Amoxicillin is not effective against β-lactamase–producing bacteria. Clavulanate, a β-lactamase inhibitor, has weak antibacterial activity but is a potent inhibitor of plasmid-mediated β-lactamases and protects amoxicillin from degradation by β-lactamases.

Drug Characteristics: Amoxicillin/Clavulanate

Dose Adjustment Hepatic	Consider dose adjustment in severe impairment	**Absorption**	F = 85%, no effect of food on absorption
Dose Adjustment Renal	CrCl 10-30 mL/min, increase interval to q12h; CrCl <10 mL/min, increase interval to q24h; avoid 875 mg tablet and extended-release tablet for those on hemodialysis or CrCl <30 mL/min	**Distribution**	17-20% protein bound. Lung, pleural f uid, bile, liver, and inner ear
Dialyzable	Yes (peritoneal and hemodialysis)	**Metabolism**	Amoxicillin not metabolized, extensive metabolism of clavulanic acid
Pregnancy Category	B	**Elimination**	Renal elimination of amoxicillin is 50-70% with a half-life of 1-2 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to penicillins, extended-release products are contraindicated in patients on dialysis or severe renal dysfunction	**Black Box Warnings**	None

Medication Safety Issues: Amoxicillin/Clavulanate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Augmentin XR, ES 600	No	Extended-release tablet	No	Amoxicillin	No

Drug Interactions: Amoxicillin/Clavulanate

Typical Agents	Mechanism	Clinical Management
Methotrexate	Decreased methotrexate clearance	Avoid concurrent use or consider methotrexate dose reduction or monitoring levels
Venlafaxine	Increased risk or serotonin syndrome	Avoid concurrent use
Warfarin	Increased risk of bleeding	Increase warfarin monitoring

Adverse Reactions: Amoxicillin/Clavulanate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, diarrhea	Skin rash, vomiting, mycosis, candidiasis	Severe hypersensitivity, renal failure, hepatic failure, pancytopenia

Efficacy Monitoring Parameters. Resolution of clinical signs of infection.

Toxicity Monitoring Parameters. Severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

Key Patient Counseling Points. Complete full course of therapy. Take dose with food to ensure proper absorption. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution of 10 d. Avoid mixing suspension with food or beverages. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

Clinical Pearls. There is cross-hypersensitivity between penicillin and cephalosporin; use with caution in cephalosporin-allergic patients. Incidence of diarrhea is higher than with amoxicillin alone. May decrease effectiveness of oral contraceptives.

ANASTROZOLE: Arimidex, Various

Class: Aromatase Inhibitor

Dosage Forms. Tablet: 1 mg

Astra Zeneca 1 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Breast cancer, adjuvant, postmenopausal, hormone receptor-positive: 1 mg po daily × 5 y
2. Breast cancer, advanced or metastatic, postmenopausal, following tamoxifen therapy: 1 mg po daily, until tumor progression

Off-Label Uses.

1. Breast cancer, neoadjuvant, postmenopausal, hormone receptor-positive: 1 mg po daily for 3-6 mo
2. Breast cancer, prophylaxis, postmenopausal women at high risk: 1 mg po daily × 5 y

MOA. Adrenally generated androstenedione is the primary source of estrogen in postmenopausal women and is converted to estrone by aromatase. Anastrozole is a nonsteroidal aromatase inhibitor.

Drug Characteristics: Anastrozole

Dose Adjustment Hepatic	Severe, use with caution	**Absorption**	F = 80%, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 300-500 L; 40% protein bound
Dialyzable	Unknown	**Metabolism**	85% metabolism but not by CYP
Pregnancy Category	X	**Elimination**	Renal elimination is 10% with a half-life of 50 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity and pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Anastrozole

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Aromasin, letrozole	No

Drug Interactions: Anastrozole

Typical Agents	Mechanism	Clinical Management
Tamoxifen	Reduced anastrozole levels	Avoid concurrent use

Adverse Reactions: Anastrozole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, hypertension, vasodilation, nausea, vomiting, arthralgia, arthritis, osteoporosis, hot f ashes, depression, GI tract disorder	Angina, chest pain, thrombophlebitis, alopecia, pruritus, rash, weight gain, hyperlipidemia, xerostomia, elevated LFTs, thromboembolic events, ischemic cardiovascular disease, diarrhea, elevated serum cholesterol	Myocardial infarction, endometrial cancer, cerebrovascular accident

Efficacy Monitoring Parameters. Decrease in tumor size if used in metastatic or neoadjuvant setting. Absence of tumor recurrence if used in adjuvant setting.

Toxicity Monitoring Parameters. BP, cholesterol panel, BMD panel (serum albumin, calcium and alkaline phosphatase, and phosphate and osteocalcin measurements), dual-energy x-ray absorptiometry for monitoring osteoporosis.

Key Patient Counseling Points. Seek medical attention if shortness of breath, swelling, chest pain, vaginal bleeding, blistering rash, rapid weight gain, severe nausea and vomiting, yellowing of the eyes or skin. Take with or without food. Because anastrozole lowers level of estrogen, can lead to loss of BMD and increase risk of fractures.

Clinical Pearls. As effective as tamoxifen in treating metastatic breast cancer, but decreased incidence of adverse effects (thromboembolic events and endometrial cancer). Not indicated in premenopausal women.

ARIPIPRAZOLE: Abilify

Class: Antipsychotic

Dosage Forms. Tablet: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg; **Tablet (Disintegrating):** 10 mg, 15 mg; **Solution:** 1 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disorder, manic or mixed episodes: Adults, 2 mg po daily, may titrate to 15-30 mg po daily; Children >10 y, 2 mg po daily, may titrate to 10 mg po daily
2. Schizophrenia: Adults, 10-15 mg po daily, may titrate to *max* 30 mg/d; Children >13 y, 2 mg po daily, may titrate to 10 mg po daily
3. Depression, adjunctive with antidepressant: 2-4 mg po daily, may titrate to 15 mg po daily

Bristol-Myers Squibb 15 mg pictured

Off-Label Uses. None

MOA. Aripiprazole is an atypical antipsychotic agent (quinolinone derivative). It exhibits relatively high affinity for dopamine D_2 and D_3 receptors and serotonin 5-HT_{1A} and 5-HT_{2A} receptors.

Drug Characteristics: Aripiprazole

Dose Adjustment Hepatic	Not required	**Absorption**	F = 87%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 4.9 L/kg; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, 80%; major substrate of CYP2D6 and 3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 10-20% with a half-life of 75-94 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 poor metabolizers should receive 50% lower dose
Contraindications	Hypersensitivity	**Black Box Warnings**	Dementia, suicidality

Medication Safety Issues: Aripiprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	ARIPiprazole	No	No	Omeprazole, pantoprazole, RABEprazole	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others

Drug Interactions: Aripiprazole

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased aripiprazole metabolism reduces aripiprazole effectiveness	Use with caution; monitor efficacy. Consider aripiprazole dose increase of 50%
CYP3A4/5, 2D6 inhibitors	Decreased aripiprazole metabolism increases risk of aripiprazole toxicity	Initiate aripiprazole at 50% lower doses; monitor for side effects

Adverse Reactions: Aripiprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Akathisia, anxiety, extrapyramidal disease, headache, increased appetite, somnolence, weight gain	Blurred vision, constipation, diarrhea, dizziness, excessive salivation, fatigue, hyperglycemia, insomnia, nausea, orthostatic hypotension, rash, restlessness, somnolence, tremor, vomiting, xerostomia	Neuroleptic malignant syndrome, pancytopenia, QT prolongation, seizures, suicidal thoughts, tardive dyskinesia

Efficacy Monitoring Parameters. Improvement in mental status (schizophrenia, mania, depression symptoms).

Toxicity Monitoring Parameters. FPG and CBC prior to treatment and periodically in patients with risk factors for diabetes. Patients at high risk for suicide should be closely supervised during therapy. Monitor ECG at baseline and periodically during therapy.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Drug may impair heat regulation. Drug may also lower seizure threshold. Patients with history of seizures or conditions that lower seizure threshold should report increased seizure activity. Report worsening depression, suicidal ideation, or unusual changes in behavior, especially at initiation of therapy or with dose changes. Children, adolescents, and young adults are at higher risk for these effects during the first few months of therapy. Report signs/symptoms of hyperglycemia, extrapyramidal effects, and neuroleptic malignant syndrome. Avoid sudden discontinuation. Avoid alcohol.

Clinical Pearls. Solution may be substituted for the tablet dosages on an mg-per-mg basis for up to a 25-mg dose; patients on 30-mg tablets should receive 25 mg of the solution. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Injectable formulation also available.

ATAZANAVIR: Reyataz

Class: Antiretroviral Agent, Protease Inhibitor

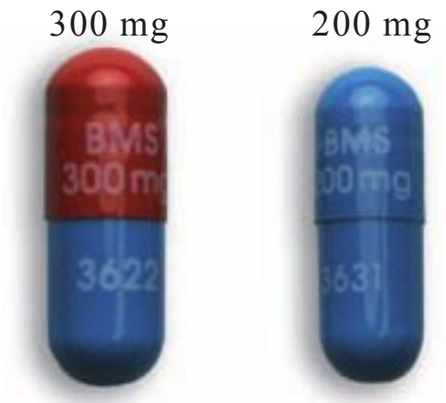
Dosage Forms. Capsule: 150 mg, 200 mg, 300 mg

Common FDA Label Indication, Dosing, and Titration.

1. Treatment of HIV-1 infections in combination with at least 2 other antiretroviral agents: Adults and Children ≥13 y of age and ≥40 kg, 300-400 mg po daily; Children <13 y of age, weight based and used in combination with ritonavir

Off-Label Uses. None

MOA. Binds to the site of HIV-1 protease activity and inhibits cleavage of viral Gag-Pol polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles.



Bristol-Myers Squibb pictured

Drug Characteristics: Atazanavir

Dose Adjustment Hepatic	Use with caution if moderate hepatic impairment	**Absorption**	F approaches 100%, food increases absorption by 50%
Dose Adjustment Renal	Not required	**Distribution**	CSF and semen
Dialyzable	Yes	**Metabolism**	Hepatic; substrate of CYP3A4/5, strong inhibitor of CYP3A4/5 and UGT1A1
Pregnancy Category	B	**Elimination**	80% hepatic, with half-life of 7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Resistance is associated with HIV mutations
Contraindications	Hypersensitivity or concurrent therapy with alfuzosin, cisapride, ergot derivatives indinavir, irinotecan, lovastatin, midazolam (oral), pimozide, rifampin, sildenafil, simvastatin, or triazolam	**Black Box Warnings**	None

Medication Safety Issues: Atazanavir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not open capsule	Yes	No	No

Drug Interactions: Atazanavir

Typical Agents	Mechanism	Clinical Management
Antacids	Decreased absorption of atazanavir	Separate use by 2 h
CYP3A4/5 inhibitors	Decreased metabolism and increased toxicity of atazanavir	Avoid strong inhibitors, monitor and dose reduce atazanavir with concurrent moderate or weak inhibitors
CYP3A4/5 inducers	Increased metabolism and decreased efficacy of atazanavir	Avoid
CYP3A4/5 substrates	Decreased metabolism and increased toxicity of CYP3A4/5 substrates via inhibition of CYP3A4/5	Avoid sensitive CYP3A4/5 substrates
Drugs that prolong PR or QT	Additive PR or QT prolongation and cardiotoxicity	Avoid or monitor ECGs
Oral contraceptives	Reduced efficacy of oral contraceptives, unknown mechanism	Use an alternative form of contraception
Proton pump inhibitors, H_2 antagonists	Decreased absorption of atazanavir	Avoid
UGT1A1 substrates	Decreased metabolism and increased toxicity of UGT1A1 substrates via inhibition of UGT1A1	Avoid sensitive UGT1A1 substrates

Adverse Reactions: Atazanavir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Rash, hyperlipidemia, elevated LFTs, abdominal pain, elevated bilirubin level, cough, fever	Nausea, vomiting, diarrhea, headaches, hyperglycemia, nausea, AV block, peripheral edema	Hypersensitivity, renal failure, PR and QT prolongation, torsades de pointes, cholelithiasis, left bundle branch block

Efficacy Monitoring Parameters. HIV viral load, CD4 count, drug levels with some concomitant medications.

Toxicity Monitoring Parameters. LFTs, bilirubin, ECG monitoring in patients with prolonged PR interval or with concurrent AV nodal blocking drugs, CBCs, lipid panel.

Key Patient Counseling Points. Multiple, potentially serious drug interactions; do not take new medications without consulting health-care provider. Take with food. Do not open, chew, or crush capsule. Does not prevent transmission of HIV; practice safe sex. Do not skip doses. Report cardiac symptoms to physician. Do not take antacids within 2 h of this medication.

Clinical Pearls. Not recommended for infants <3 mo of age. Atazanavir dose varies with concurrent medications, pregnancy, and prior HIV therapy.

ATENOLOL: Tenormin, Various

A

Class: β-Adrenergic Blocker, Cardioselective

Dosage Forms. Tablet: 25 mg, 50 mg, 100 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Angina pectoris, chronic: 50 mg po daily; titrate to 100-200 mg po daily
2. Hypertension: Adults, 50 mg po daily, titrate to 100 mg po daily; Children, 0.5-1 mg/kg/d po in 1-2 divided doses, titrate to 2 mg/kg/d po in 1-2 divided doses (*max* 100 mg/d)

Off-Label Uses.

1. Cardiac dysrhythmia: Adults, 50-100 mg po daily; Children, 0.3-1.4 mg/kg po daily, titrate to 2 mg/kg po daily
2. Migraine prophylaxis: 50-100 mg po daily

MOA. Atenolol is a cardioselective β-adrenergic that decreases AV nodal conduction in supraventricular tachycardias and blockade of catecholamine-induced dysrhythmias.

Drug Characteristics: Atenolol

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50%; food decreases AUC by 20%
Dose Adjustment Renal	CrCl 15-35 mL/min, *max* dose 50 mg po daily; CrCl <15 mL/min, *max* dose 25 mg po daily	**Distribution**	Vd = 50-75 L; <5% protein bound
Dialyzable	Yes, give 25-50 mg after each dialysis procedure	**Metabolism**	Not metabolized
Pregnancy Category	D	**Elimination**	Renal elimination of atenolol is 40-50% and 50% in feces as unchanged drug, with a half-life of 6-7 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to atenolol, severe sinus bradycardia, 2nd- or 3rd-degree AV block, overt heart failure or cardiogenic shock	**Black Box Warnings**	Avoid abrupt withdrawal

Medication Safety Issues: Atenolol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Albuterol	No

Drug Interactions: Atenolo

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of atenolol	Avoid concurrent use or monitor blood pressure
Amiodarone, dronedarone	Increased risk of bradycardia, heart block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
Antidiabetic drugs	Decreased glycemic control	Monitor blood glucose levels
Calcium channel blockers, quinidine	Increased risk of hypotension and/or bradycardia and AV block	Avoid concurrent use
Clonidine	Exaggerated clonidine withdrawal response	Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy
Digoxin	Increased risk of AV block	Monitor HR, ECG, and serum digoxin concentrations
Alpha-blockers, fentanyl	Increased risk of hypotension	Monitor blood pressure

Adverse Reactions: Atenolol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bradyarrhythmias, cold extremities, dizziness, fatigue, hypotension, depression	Bronchospasm, dyspnea, somnolence, sexual dysfunction	Heart failure, pulmonary embolism

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes and renal function at baseline and periodically.

Key Patient Counseling Points. Take on an empty stomach and avoid alcohol. Avoid abrupt discontinuation; exacerbations of angina may occur. Report signs/symptoms of hypotension, heart failure, or exacerbation of angina with initial dosing and dose changes. May cause dizziness or drowsiness. Diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia.

Clinical Pearls. Safety and efficacy not established in children. Full effectiveness may not be seen for 1-2 wk. Taper slowly before stopping as sudden discontinuation can cause angina or MI.

ATOMOXETINE: Strattera

Class: Norepinephrine Reuptake Inhibitor, CNS Stimulant

Dosage Forms. Capsule: 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg

Lilly pictured

Common FDA Label Indication, Dosing, and Titration.

1. ADHD: Children >6 y of age and weighing ≤70 kg, 0.5 mg/kg/d po, may titrate to lower of 1.4 mg/kg/d or 100 mg/d; Children >6 y of age and weighing >70 kg, 40 mg/d po, may titrate to 100 mg/d; Adults, 40 mg po daily, may titrate to 100 mg/d

Off-Label Uses. None

MOA. Atomoxetine is a selective norepinephrine reuptake inhibitor that produces therapeutic effects in patients with ADHD. The exact mechanism of how selective inhibition of presynaptic norepinephrine exerts effects in ADHD has not been determined.

Drug Characteristics: Atomoxetine

Dose Adjustment Hepatic	Child-Pugh Class B: initial and target doses should be reduced to 50% of normal dose; Child-Pugh Class C: initial and target doses should be reduced to 25% of normal dose	**Absorption**	F = 63% (normal metabolizers); 94% (poor metabolizers); food does not affect absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.85 L/kg; 98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism to 1 active metabolite; major substrate of CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 80% and 17% in feces, with a half-life of 5.2-21.6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 poor metabolizers, dose as with drug interaction with CYP2D6 inhibitor
Contraindications	Hypersensitivity to atomoxetine; concomitant use of MAOIs or use within 2 wk; narrow-angle glaucoma, pheochromocytoma	**Black Box Warnings**	Suicidality in children and adolescents

Medication Safety Issues: Atomoxetine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	AtoMOXetine	Do not open capsules	No	AtorvaSTATin	No

Drug Interactions: Atomoxetine

Typical Agents	Mechanism	Clinical Management
CYP2D6 inhibitors	Decreased atomoxetine metabolism increases risk of atomoxetine toxicity	Children >6 y of age weighing >70 kg, dose 0.5 mg/kg/d po, may titrate up to 1.2 mg/kg/d; Children >6 y of age weighing >70 kg, dose 40 mg po daily, may titrate to 80 mg/d
Albuterol	Increased HR	Monitor BP and HR
MAOIs	Increased risk of hypertensive crisis (headache, hyperpyrexia, hypertension)	Concomitant use contraindicated

Adverse Reactions: Atomoxetine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Abdominal pain, headache, insomnia, loss of appetite, nausea, weight loss, xerostomia	Agitation, anxiety, decreased growth and development, dysmenorrhea, erectile dysfunction, increased blood pressure, rash, somnolence, urinary retention, vomiting, weight loss	Dyskinesia, mania, prolonged QT interval, psychotic disorders, seizure, suicidal thoughts, sudden cardiac death, tachycardia, hepatotoxicity

Efficacy Monitoring Parameters. Improvement of mental and behavioral symptoms of ADHD.

Toxicity Monitoring Parameters. BP and HR. Signs of clinical worsening, suicidality, or unusual changes in behavior; particularly at start of and during first few months of therapy or when dose is adjusted. Aggressive behavior or hostility, new onset or worsening; in pediatric patients at start of treatment.

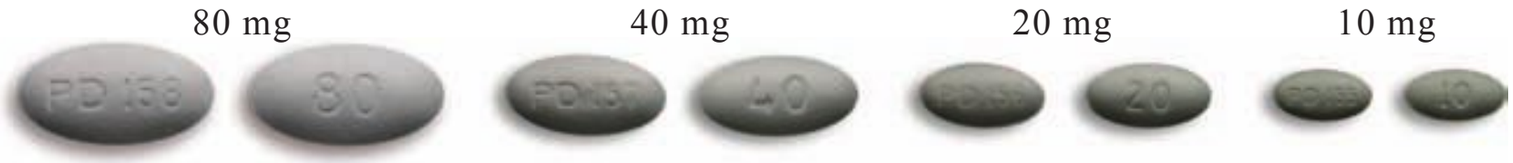
Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Growth rate and weight may need to be monitored more frequently in children. Report new or worsened psychiatric problems, chest pain, palpitations, dyspnea, or signs/symptoms of cardiac dysrhythmias, MI, or cerebrovascular accident. Do not open capsules as atomoxetine is an ocular irritant.

Clinical Pearls. Safety and effectiveness not established in children <6 y of age. Increased risk of suicidal ideation in short-term studies in children or adolescents with ADHD. Monitor patients closely for suicidality (suicidal thinking and behavior), clinical worsening, or unusual changes in behavior. Close observation and communication with the prescriber by families and caregivers is recommended.

ATORVASTATIN: Lipitor, Various

Class: HMG-CoA Reductase Inhibitor

Dosage Forms. Tablet: 10 mg, 20 mg, 40 mg, and 80 mg



Pfizer pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hyperlipidemia: 10-20 mg po daily, may increase to 80 mg po daily
2. Primary and secondary prevention of atherosclerotic cardiovascular disease: 20-40 mg po daily, may increase to 80 mg po daily for those patients requiring high-intensity therapy (eg, LDL >190 mg/dL)
3. Secondary prevention of cardiovascular events in patients with or at high risk for CAD: 80 mg daily, may reduce dose to 40 mg po daily if high dose not tolerated
4. Familial hypercholesterolemia (homozygous): Children (boys and postmenarchal girls aged 10-17 y), 10 mg po daily, may titrate to 40 mg po daily; Adults 10-80 mg po daily

Off-Label Uses. None

MOA. HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol also can decrease because of decreased production of VLDL-cholesterol or increased VLDL; removal by LDL receptors.

Drug Characteristics: Atorvastatin

Dose Adjustment Hepatic	Avoid use in patients with active liver disease or unexplained persistent elevated LFTs	**Absorption**	F = 14%; food slows rate of absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 381 L; 98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP3A4/5 and P-glycoprotein; inhibits P-glycoprotein
Pregnancy Category	X	**Elimination**	Biliary elimination, renal elimination 1-2%, with a half-life of 7-14 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	LDL receptor alters efficacy
Contraindications	Hypersensitivity to atorvastatin, pregnancy or lactation	**Black Box Warnings**	None

Medication Safety Issues: Atorvastatin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	AtorvaSTATin	No	No	AtoMOXetine, lovastatin, nystatin, pravastatin, simvastatin	No

Drug Interactions: Atorvastatin

Typical Agents	Mechanism	Clinical Management
Aliskiren	Increased aliskiren concentrations and risk of toxicity	Monitor for hypotension
CYP3A4/5 inducers	Increased atorvastatin metabolism reduces atorvastatin effectiveness	Monitor fasting lipid panels
CYP3A4/5 inhibitors	Decreased atorvastatin metabolism increases risk of atorvastatin toxicity	Avoid concurrent use or monitor for myopathy and measure CK levels; *max* dose 20 mg/d
Clopidogrel	Decreased antiplatelet activity of clopidogrel by atorvastatin	Avoid concurrent use
Cyclosporine, HIV protease inhibitors, hepatitis C protease inhibitors	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use
P-glycoprotein substrates	Metabolism of P-glycoprotein substrates inhibited by atorvastatin, resulting in substrate toxicity	Monitor for adverse effects and reduce substrate dose if necessary

Adverse Reactions: Atorvastatin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Arthralgia, diarrhea, headache	Increased liver enzymes, indigestion, insomnia, musculoskeletal pain, myalgia, nasopharyngitis, nausea, increased hemoglobin A1c	Rhabdomyolysis, tendon rupture

Efficacy Monitoring Parameters. Total cholesterol, LDL-cholesterol, and triglycerides levels; HDL-cholesterol levels.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs should be performed at baseline, 12 wk after initiation of therapy, and every 6 mo thereafter; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

Key Patient Counseling Points. Contact prescriber immediately if pregnancy occurs while taking atorvastatin. Avoid alcohol, grapefruit, and grapefruit juice while taking drug. Atorvastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

Clinical Pearls. Lipid level assessment should be done within 6-12 wk following dose initiation or titration, then every 3-12 mo. If 2 consecutive LDL levels are <40 mg/dL, consider decreasing dose. Statins have been reported to increase risk of diabetes, although this data is controversial as statins are only associated with very mild increase in blood glucose and there is no established causal relationship.

AZELASTINE: Astelin, Astepro, Various

A

Class: Nasal Antihistamine

Dosage Forms. Nasal Spray: 0.15%, 137 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Perennial allergic rhinitis: Adults and Children ≥12 y of age, 2 sprays per nostril bid; Children 6-12 y of age, 1 spray per nostril bid
2. Seasonal allergic rhinitis: Adults and Children ≥12 y of age 1-2 sprays per nostril bid; Children 6-12 y of age, 1 spray per nostril bid
3. Vasomotor rhinitis: Adults and Children ≥12 y of age, 2 sprays per nostril bid

Off-Label Uses. None

MOA. Azelastine is a selective H_1-receptor antagonist that blocks release of histamine from cells involved in the allergic response. It also inhibits other mediators of allergic reactions (eg, leukotrienes, etc), and reduces chemotaxis and eosinophil activation.

Drug Characteristics: Azelastine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40% when administered nasally
Dose Adjustment Renal	Not required	**Distribution**	Vd = 14.5 L/kg; 78-95% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, 90%
Pregnancy Category	C	**Elimination**	Fecal elimination is 75% with a half-life of 22-25 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Meda pictured

Medication Safety Issues: Azelastine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Astelin and Astepro	No

Drug Interactions: Azelastine

Typical Agents	Mechanism	Clinical Management
Cimetidine	Inhibition of azelastine metabolism	Avoid concurrent use or monitor for increased azelastine adverse effects

Adverse Reactions: Azelastine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bitter taste in mouth, headache, somnolence	Fatigue, epistaxis, pharyngitis, rhinitis, sneezing	

Efficacy Monitoring Parameters. Decrease in rhinitis symptoms.

Toxicity Monitoring Parameters. Seek medical attention if severe allergic reactions occur.

Key Patient Counseling Points. Avoid spraying in eyes. Somnolence has been reported with nasal administration; instruct patient to avoid alcohol use and hazardous activities such as driving or operating machinery until level of sedation is known. Review proper instillation technique, including priming the spray with initial use and if have not used for 3 or more days. Blow nose prior to using. Do not spray into wall separating nostrils. To prevent contamination, keep tip of nose spray clean.

Clinical Pearls. Also available as ophthalmic product for ocular rhinitis symptoms. Also available in nasal product in combination with fluticasone.

AZITHROMYCIN: Zithromax, Various

Class: Macrolide Antibiotic

Dosage Forms. Oral Tablet: 250 mg, 500 mg, 600 mg; **Microspheres for Suspension:** 2 g/bottle; **Powder for Oral Suspension:** 100 mg/5 mL, 200 mg/5 mL, 1 g packet

Wockhardt generic 250 mg pictured

Teva generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute infective exacerbation of COPD, skin or tissue infection: 500 mg po daily × 3 d or 500 mg po × 1 dose, then 250 mg po daily × 2-5 d
2. Bacterial sinusitis: Adults, 500 mg po daily × 3 d; Children, 10 mg/kg po daily × 3 d, or 2 g po × 1 dose
3. Chancroid, nongonococcal cervicitis, nongonococcus urethritis: 1 g po × 1 dose
4. Community-acquired pneumonia: 500 mg po daily × 3 d or 500 mg po × 1, then 250 mg po daily × 2-5 d; Infants ≥6 mo of age, tablets and immediate-release suspension, 10 mg/kg po on day 1, then 5 mg/kg po daily × 2-5 d *or* extended-release suspension, <34 kg, 60 mg/kg po × 1; >34 kg, 2 g po × 1 dose
5. Gonorrhea, urethritis, or cervicitis: 2 g po × 1 dose
6. Streptococcal pharyngitis: 500 mg po × 1 dose, then 250 mg po daily × 2-5 d; Children, 12 mg/kg po daily × 5 d

Other Uses.

1. Traveler's diarrhea: Adults, 1000 mg po × 1 dose, or 500 mg po daily × 3 d; Children, 10 mg/kg po daily × 3 d
2. Bacterial endocarditis, prophylaxis: Adults, 500 mg po 30-60 min prior to procedure; Children, 15 mg/kg po 30-60 min prior to procedure

MOA. Azithromycin is a macrolide antibiotic that is slightly less active than erythromycin against gram-positive bacteria but substantially more active against *M.* (*B.*) *catarrhalis, Haemophilus* sp., *Legionella* sp., *Neisseria* sp., *Bordetella* sp., *Mycoplasma* spp., and *C. trachomatis*. Azithromycin binds to the 50S ribosomal subunit, thus interfering with microbial protein synthesis.

Drug Characteristics: Azithromycin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 38%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Blister f uid, bronchial secretions, cervix, ear f uid, ovaries, sputum, soft tissue
Dialyzable	Not dialyzable	**Metabolism**	Hepatic
Pregnancy Category	B	**Elimination**	Renal elimination is 6% with a half-life of 68 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to azithromycin, erythromycin, or any macrolide or ketolide antibiotic	**Black Box Warnings**	None

Medication Safety Issues: Azithromycin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Azathioprine, erythromycin, Fosamax	No

Drug Interactions: Azithromycin

Typical Agents	Mechanism	Clinical Management
Agents that prolong the QT interval and class III antiarrhythmics	Additive cardiotoxicity	Avoid concurrent use
Statins	Increased risk of rhabdomyolysis; mechanism unknown	Use caution with concurrent use
Digoxin	Increased digoxin toxicity via decreased bacterial metabolism of digoxin in the lower intestine	Use caution with concurrent use
Ergot alkaloids	Increased risk of acute ergotism via inhibition of ergot metabolism	Contraindicated
Nelfinavir	Increased azithromycin concentrations via decreased clearance	Caution with concurrent use
Warfarin	Increased risk of bleeding via inhibition of warfarin metabolism	Monitor INR closely

Adverse Reactions: Azithromycin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea, vomiting, abdominal pain	Headache, elevated liver enzymes, flatulence	Stevens-Johnson syndrome, chest pain, severe hypersensitivity, myasthenia gravis, QT prolongation, torsades de pointes, hepatitis

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Seek medical attention if chest pain, blistering skin rash, or extreme fatigue.

Key Patient Counseling Points. Complete full course of therapy. Take tablets with or without food, although some patients report increased tolerability when given with food. Avoid mixing suspension with food or beverages, but food can be taken afterward. Take extended-release suspension (Zmax) on empty stomach, at least 1 h before or 2 h after a meal. Zmax must be used in the first 12 h of reconstitution. Avoid concurrent use of aluminum or magnesium-containing antacids (exception: Zmax can be taken without regards to antacids containing magnesium hydroxide and/or aluminum hydroxide). Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

Clinical Pearls. Use with caution in severe renal, hepatic, or cardiac disease. Pediatric use of extended-release tablets is restricted to community-acquired pneumonia. Max dose in children is 500 mg. There is a small absolute increase in the risk of cardiovascular death during a 5-d course of oral azithromycin. Also available as ophthalmic for bacterial conjunctivitis, and injectable for severe infections.

BACLOFEN: Lioresal, Various

Class: Centrally Acting Skeletal Muscle Relaxant

Dosage Forms. Oral Tablet: 10 mg, 20 mg

Northstar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Spasticity: 5 mg orally tid; may increase dose in 5-15 mg/d increments; *max* dose in Adults and Children ≥12 y of age, 80 mg/d; *max* dose in children 8-12 y of age, 60 mg/d; *max* dose in children <8 y of age, 40 mg/d

Off-Label Uses.

1. Intractable hiccoughs, 5 mg po bid, increasing to 15-45 mg/d in 3 divided doses; or 10-20 mg 2-3 times daily

MOA. Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by hyperpolarization of afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is an analogue of γ-aminobutyric acid (GABA), but there is no conclusive evidence that actions on GABA systems are involved in the production of its clinical effects.

Drug Characteristics: Baclofen

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%, no effect of food on absorption
Dose Adjustment Renal	In patients with renal dysfunction, monitor carefully for toxicity and reduce dose as necessary	**Distribution**	Vd = 59.1 L; 30% protein bound
Dialyzable	Yes	**Metabolism**	Limited hepatic metabolism
Pregnancy Category	C	**Elimination**	Renal elimination is 60-80% with a half-life of 3-7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	Avoid abrupt discontinuation of intrathecal product

Medication Safety Issues: Baclofen

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes, intrathecal	Bactroban	No

Drug Interactions: **Baclofen.** None known

Adverse Reactions: Baclofen

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, asthenia, dizziness, somnolence	Constipation, fatigue, hypotension, shivering, urinary complication	Pneumonia, GI hemorrhage

Efficacy Monitoring Parameters. Reduction in muscle spasm, passive limb movement, pain relief.

Toxicity Monitoring Parameters. Seek medical attention if severe dizziness, confusion, sedation, or rebound spasticity occurs.

Key Patient Counseling Points. Because of the possibility of sedation, patients should be cautioned regarding the operation of motor vehicles or dangerous machinery while taking baclofen. Patients should be cautioned that the CNS effects of baclofen may be additive to those of alcohol and other CNS depressants.

Clinical Pearls. Implantable pumps that administer baclofen intrathecally are also available for patients with spasticity. Constipation occurs in 100% of patients undergoing intrathecal administration, and abrupt discontinuation of intrathecal therapy (intentional or inadvertent) is commonly fatal.

BENAZEPRIL: Lotensin, Various

Class: ACE-I, Antihypertensive

Dosage Forms. Oral Tablet: 5 mg, 10 mg, 20 mg, 40 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, 10 mg po daily, may titrate to 20-40 mg po daily (*max* 80 mg/d); Children ≥6 y of age, 0.2 mg/kg po daily (*max* 0.6 mg/kg/d or 40 mg/d)

Off-Label Uses.

1. Diabetic nephropathy: 10 mg po daily
2. Heart failure: 5-40 mg po daily
3. Kidney disease: 10 mg po daily

MOA. Benazepril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.

Drug Characteristics: Benazepril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 37%, no effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, initial dose is 5 mg po daily, titrate to effect (*max* 40 mg/d)	**Distribution**	Vd = 8.7 L; 97% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism to 1 active metabolite (benazeprilat)
Pregnancy Category	D	**Elimination**	Renal elimination is 33%, bile 12% with a half-life of 0.6 h (parent drug) and 22 h (benazeprilat)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity; history of angioedema; anuria; concomitant use with aliskiren in patients with diabetes mellitus	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Benazepril

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Benadryl	No

Drug Interactions: Benazepril

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Angiotensin receptor blockers (ARBs)	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium level
NSAIDs	Decrease antihypertensive and natriuretic effect of benazepril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr level
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use, monitor for anemia or leucopenia
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP, rise from seated position slowly

Adverse Reactions: Benazepril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, dizziness, dry cough, fatigue, headache, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting	Angioedema, birth defects, liver failure, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

Key Patient Counseling Points. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Take at the same time daily.

Clinical Pearls. Observe patients who are volume depleted for at least 2 h after taking the initial dose of benazepril. A liquid suspension can be made for patients who cannot swallow pills.

BENZONATATE: Tessalon Perles, Various

Class: Antitussive

Dosage Forms. **Oral Capsule, Liquid Filled:** 100 mg, 150 mg, 200 mg

Common FDA Label Indication, Dosing, and Titration.

1. Cough: Adults and Children >10 y of age, 100-200 mg po tid prn, *max* 600 mg/d

Off-Label Uses.

1. Endotracheal intubation hiccups: 100 mg po × 1 dose, may repeat in 4 h

MOA. Benzonatate acts peripherally by anesthetizing the stretch receptors located in the respiratory passages, lungs, and pleura by dampening their activity and thereby reducing the cough reflex at its source.

Amneal generic 100 mg pictured

Drug Characteristics: Benzonatate

Dose Adjustment Hepatic	Not required	**Absorption**	Unknown
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Unknown
Pregnancy Category	C	**Elimination**	Unknown
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Benzonatate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not bite, chew, or open; swallow capsule whole	No	No	No

Drug Interactions: Benzonatate. None known

Adverse Reactions: Benzonatate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
If capsules are broken or chewed, oral and pharyngeal numbness	Dizziness, headache, sedation, somnolence, bizarre behavior (mental confusion and visual hallucinations)	Severe hypersensitivity reactions

Efficacy Monitoring Parameters. Resolution of clinical signs of cough.

Toxicity Monitoring Parameters. Seek medical attention if rash or hives, itching, difficulty breathing or swallowing, confusion, or hallucinations occur.

Key Patient Counseling Points. Do not chew capsules or allow capsules to dissolve in mouth as oropharyngeal anesthesia will occur, plus the liquid in the capsule has an incredibly foul taste. Administer with food or milk if GI upset occurs. Accidental ingestion of as few as 1-2 capsules by children <2 y of age has been fatal. The drug appearance (round, clear liquid-filled capsules) may be attractive to children, so particular care should be taken to keep out of reach.

Clinical Pearls. Benzonatate was approved by the FDA in 1958. Very little pharmacologic or pharmacokinetic data exist for this product. Do not spill the bottle—will take you hours to track down capsules that are spilled.

BENZTROPINE: Cogentin, Various

Class: Antiparkinsonian, Anticholinergic

Dosage Forms. Oral Tablet: 0.5 mg, 1 mg, 2 mg

Core Pharma generic 1 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Extrapyramidal disease, medication-induced movement disorder: Adults, 1-4 mg po daily or bid; Children ≥3 y of age, 0.02-0.05 mg/kg/dose once or twice daily
2. Parkinsonism: 1-2 mg/d po, may titrate to range 0.5-6 mg/d po

Off-Label Uses. None

MOA. Benztropine possesses anticholinergic and antihistamine effects. May inhibit reuptake and storage of dopamine.

Drug Characteristics: Benztropine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 29%
Dose Adjustment Renal	Not required	**Distribution**	Protein binding unknown
Dialyzable	Not dialyzable	**Metabolism**	Unknown
Pregnancy Category	B	**Elimination**	Unknown
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to benztropine, patients <3 y of age	**Black Box Warnings**	None

Medication Safety Issues: Benztropine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Bromocriptine	Avoid

Drug Interactions: Benztropine

Typical Agents	Mechanism	Clinical Management
Amantadine	Increased CNS toxicity (confusion, hallucinations)	Monitor for signs of toxicity
Phenothiazines	Decreased phenothiazine concentrations, enhanced anticholinergic effects	Monitor for efficacy
Haloperidol	Excessive anticholinergic effects	Monitor for signs of toxicity

Adverse Reactions: Benztropine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Blurred vision, confusion, constipation, disorientation, dysuria, mydriasis, nausea, urinary retention, xerostomia	Anhidrosis, drug-induced psychosis, heat stroke, increased body temperature, tachycardia, visual hallucinations

Efficacy Monitoring Parameters. Reduction in extrapyramidal movements, rigidity, tremor, gait disturbances.

Toxicity Monitoring Parameters. Monitor for anticholinergic effects including dry mouth and constipation.

Key Patient Counseling Points. Drug may impair heat regulation. Advise patient to use caution with activities leading to an increased core temperature, such as strenuous exercise, exposure to extreme heat, or dehydration. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Instruct patient to report sudden muscle weakness or stiffness, and signs/symptoms of tardive dyskinesia (tongue thrusting, facial grimacing/tics, random movements of extremities). Patient should not drink alcohol while taking this drug.

Clinical Pearls. Benztropine may have more adverse effects than amantadine when used for Parkinson disease. Injectable formulation also available but must be administered at hospital or MD office.

BIMATOPROST: Lumigan, Latisse

Class: Prostaglandin, Antiglaucoma Agent, Cosmetic Agent for Eyelash Growth

Dosage Forms. Ophthalmic Solution: 0.01%, 0.03%

Common FDA Label Indication, Dosing, and Titration.

1. Ocular hypertension and open-angle glaucoma: 1 drop in affected eye(s) daily in the evening
2. Hypotrichosis of the eyelashes: 1 drop nightly to clean, upper eyelid margin at base of eyelashes, blot excess, repeat with new sterile applicator to opposite eyelid, do not apply to lower eyelids

Off-Label Uses. None

MOA. Bimatoprost is a synthetic prostaglandin analogue. Bimatoprost lowers intraocular pressure (IOP) by increasing the outflow of aqueous humor through both the trabecular meshwork and uveoscleral drainage systems. The exact mechanism of action for bimatoprost in stimulating eyelash growth is unknown.

Drug Characteristics: Bimatoprost

Dose Adjustment Hepatic	Not required	**Absorption**	Systemic absorption following ocular instillation is very low
Dose Adjustment Renal	Not required	**Distribution**	88% protein binding after systemic absorption
Dialyzable	Not dialyzable	**Metabolism**	Hepatic metabolism, extent unknown
Pregnancy Category	C	**Elimination**	Renal elimination is 67% with a half-life of 45 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Allergan 0.03% solution pictured

Medication Safety Issues: Bimatoprost

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Bimatoprost

Typical Agents	Mechanism	Clinical Management
Latanoprost	Increased IOP	Avoid concurrent use

Adverse Reactions: Bimatoprost

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Conjunctival hyperemia, eyelash growth, ocular pruritus	Application pigmentation changes to the eyelid, eyelash and periocular skin, abnormal hair growth, eyelid erythema, dry eye, eye irritation, photophobia	Macular retinal edema, bacterial keratitis

Efficacy Monitoring Parameters. Reduction in IOP. Desired growth of eyelashes and resulting improvement in social life.

Toxicity Monitoring Parameters. Seek medical attention if symptoms of ocular irritation are severe.

Key Patient Counseling Points. Wash your hands and remove contact lenses before using the medicine. For administration of Lumigan, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on the bottle right away. Separate from other eye drops by 5 min. For administration of Latisse, wash face and remove makeup before applying. Do not rinse eye if solution gets into the eye. Do not reuse supplied sterile applicators or use any other brush/applicator other than those supplied. Use a new applicator for second eye. Do not apply to lower lid, or more than once per day. Reinsert contact lens after 15 min.

Clinical Pearls. There is a risk of permanent increased iris pigmentation associated with instillation of this product, and with leakage of Latisse into the eye. The effect of Latisse on eyelash length, thickness, and darkness is not permanent and will return to baseline upon discontinuation of bimatoprost.

BISOPROLOL: Zebeta, Various

Class: Cardioselective β-Adrenergic Blocker

Dosage Forms. Oral Tablet: 5 mg, 10 mg

Sandoz generic 5 mg pictured

Sandoz generic 10 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: 2.5-5 mg po daily, may titrate to *max* of 20 mg po daily

Off-Label Uses.

1. Angina: 5-20 mg po daily
2. Atrial fibrillation: 2.5-10 mg po daily
3. Heart failure: 1.25-10 mg po daily

MOA. Bisoprolol is a cardioselective β-adrenergic blocker that decreases AV nodal conduction in supraventricular tachycardia and blockade of catecholamine-induced dysrhythmias. The antihypertensive mechanism is unknown, but contributing factors are, renin blockade, and decreases in myocardial contractility and cardiac output.

Drug Characteristics: Bisoprolol

Dose Adjustment Hepatic	Initiate with 2.5 mg po daily, may titrate to *max* of 10 mg po daily	**Absorption**	F = 80%; food has no effect on absorption
Dose Adjustment Renal	Initiate with 2.5 mg po daily, may titrate to *max* of 10 mg po daily	**Distribution**	Protein binding 30%; distribution limited to extracellular f uid space and kidneys
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP3A4/5
Pregnancy Category	C	**Elimination**	Eliminated 50% unchanged in urine with a half-life of 9-12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to bisoprolol, severe sinus bradycardia, 2nd- or 3rd-degree AV block, overt heart failure, cardiogenic shock	**Black Box Warnings**	None

Medication Safety Issues: Bisoprolol

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	DiaBeta, Zetia	No

Drug Interactions: Bisoprolol

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased bisoprolol metabolism reduces bisoprolol effectiveness	Monitor and consider dose increases of bisoprolol
CYP3A4/5 inhibitors	Decreased bisoprolol metabolism increases risk of bisoprolol toxicity	Monitor and consider dose decreases of bisoprolol
NSAIDs	Decreased antihypertensive effect of bisoprolol	Avoid concurrent use or monitor BP
Antidiabetic drugs	Decreased glycemic control	Monitor FBG
Calcium channel blockers, amiodarone, dronedarone	Increased risk of hypotension and/or bradycardia and AV block	Avoid concurrent use
Clonidine	Exaggerated clonidine withdrawal response	Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy
Digoxin	Increased risk of AV block	Monitor heart rate, ECG, and serum digoxin concentrations
Alpha-blockers, ACE-Is, fentanyl	Increased risk of hypotension	Monitor BP

Adverse Reactions: Bisoprolol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bradyarrhythmias, cold extremities, dizziness, fatigue, hypotension	Anorexia, bronchospasm, dyspnea, depression, diarrhea, headache, hyperglycemia, hyperuricemia, hypokalemia, hyponatremia, nausea, orthostatic hypotension, rash, somnolence, sexual dysfunction, vomiting	Heart failure

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased heart rate, ECG. Baseline and periodic serum, and urine electrolytes; renal function; uric acid and FBG.

Key Patient Counseling Points. Instruct patient to report signs/symptoms of dyspnea, hypotension, or heart failure. May cause dizziness; avoid alcohol, CNS depressants, or activities that require alertness. Rise slowly from a sitting/supine position, as drug may cause orthostatic hypotension. Avoid abrupt discontinuation, may cause rebound hypertension. Recommend avoiding NSAIDs while taking this drug.

Clinical Pearls. Safety in children has not been established.

BRIMONIDINE: Alphagan P, Various

Class: Adrenergic Agonist; Antiglaucoma Agent

Dosage Forms. Ophthalmic Solution: 0.1%, 0.15%, 0.2%

Common FDA Label Indication, Dosing, and Titration.

1. Ocular hypertension: 1 drop in affected eye(s) q8h, strength chosen based on therapeutic effect
2. Open-angle glaucoma: 1 drop in affected eye(s) q8h, strength chosen based on therapeutic effect

Off-Label Uses.

1. Capsulotomy of posterior lens capsule: 1 drop of 0.2% solution in operative eye 1 h prior to surgery, then 1 drop in operative eye immediately following procedure

MOA. Brimonidine, a relatively selective α-adrenergic agonist, reduces aqueous humor production and increases uveoscleral outflow. It is used to lower IOP in open-angle glaucoma or ocular hypertension.

Allergan 0.15% solution pictured

Drug Characteristics: Brimonidine

Dose Adjustment Hepatic	Not required	**Absorption**	Minor systemic absorption following ocular instillation
Dose Adjustment Renal	Not required	**Distribution**	Effective penetration of brimonidine into aqueous humor
Dialyzable	Not dialyzable	**Metabolism**	24% and occurs by unknown enzymes
Pregnancy Category	B	**Elimination**	Renal elimination is 74% with a half-life of 3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to brimonidine, concurrent MAOIs, age <2 y	**Black Box Warnings**	None

Medication Safety Issues: Brimonidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Bromocriptine	No

Drug Interactions: Brimonidine

Typical Agents	Mechanism	Clinical Management
MAOIs	Increased risk of CNS depression	Avoid concurrent use

Adverse Reactions: Brimonidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Allergic conjunctivitis, conjunctival discoloration	Burning sensation in eye, hypertension, xerostomia, somnolence, hypersensitivity reaction, visual disturbance	Syncope, arrhythmias

Efficacy Monitoring Parameters. Reduction in IOP.

Toxicity Monitoring Parameters. Seek medical attention if syncope occurs or if symptoms of ocular irritation are severe.

Key Patient Counseling Points. Wash your hands and remove contact lenses before using the medicine. For administration, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on bottle right away. Reinsert contacts after 15 min. Separate administration of other ophthalmic agents by 5 min.

Clinical Pearls. This agent has no specific advantage over other similar products for the reduction in IOP in chronic ocular hypertension or in the treatment of glaucoma. Topical product available for treatment of rosacea.

BUDESONIDE: Pulmicort Respules, Pulmicort Flexhaler, Various

Class: Inhaled Corticosteroid

Dosage Forms. **Inhalation Suspension:** 0.25 mg/2 mL, 0.5 mg/2 mL, 1 mg/2 mL; **Metered-Dose Inhaler (MDI):** 90 mcg/actuation, 180 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Asthma: Children 1-8 y of age with no previous inhaled corticosteroid therapy, 0.5 mg inhaled via nebulization in 1 or 2 divided doses; Children 1-8 y of age previously treated with corticosteroids, 0.5 mg inhaled via nebulization daily or bid, may titrate to 1 mg/d; Children >8 y of age and Adults, 180-360 mcg bid via MDI, *max* 720 mcg bid via MDI

Off-Label Uses. None

MOA. Budesonide is an anti-inflammatory with potent glucocorticoid and weak mineralocorticoid activity. It exhibits a broad range of active inhibition against multiple cell types and mediators involving allergic and nonallergic/irritant-mediated inflammation.

Drug Characteristics: Budesonide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 6%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3 L/kg; protein binding 85-90%
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP3A4/5
Pregnancy Category	B	**Elimination**	Renal elimination 60%, fecal elimination 15-29%, with a half-life of 2-3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to budesonide; hypersensitivity to milk proteins (Flexhaler); primary treatment of status asthmaticus or other acute episodes of asthma	**Black Box Warnings**	None

AstraZeneca pictured

B

Medication Safety Issues: Budesonide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Budesonide

Typical Agents	Mechanism	Clinical Management
Azole antifungals and macrolides	Increase budesonide concentrations	Avoid long-term concomitant therapy with budesonide
CYP3A4/5 inducers	Increased budesonide metabolism reduces budesonide effectiveness	Monitor and consider dose increases of budesonide
CYP3A4/5 inhibitors	Decreased budesonide metabolism increases risk of budesonide toxicity	Monitor and consider dose decreases of budesonide

Adverse Reactions: Budesonide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Upper respiratory tract infections	Cough, diarrhea, dysphonia, headache, nausea, oral candidiasis, throat irritation	Cataracts, decreased body growth, decreased bone mineral density

Efficacy Monitoring Parameters. Monitor PFTs. Resolution of asthma symptoms (symptoms, number of exacerbations, nighttime awakenings, need for rescue albuterol).

Toxicity Monitoring Parameters. Growth velocity in pediatric patients during prolonged therapy.

Key Patient Counseling Points. Advise patient on proper inhalation technique. Gently swirl nebulizer suspension before use. Use entire vial of inhalation suspension immediately after opening to avoid contamination; deliver over 5-15 min using a jet nebulizer with mouthpiece or face mask. After administration, rinse mouth with water and spit, and wash face to minimize risk of developing oral candidiasis. Provided as a strip of 5 small plastic containers with sealed caps; each container holds 1 dose. The strip of containers is sealed inside a foil pouch. Keep any unused containers inside the pouch. Once foil pouch is opened, the containers will only be good for 2 wk.

Clinical Pearls. This drug is not indicated for acute asthma attacks. Respules indicated only in children; budesonide in MDI form available for treatment of older children and adults. Also available in rectal and nasal formulations, and in MDI in combination with formoterol. Oral tablets and capsules available for systemic treatment of Crohn disease and ulcerative colitis.

BUDESONIDE/FORMOTEROL: Symbicort

Class: Inhaled Corticosteroid/Bronchodilator Combination

Dosage Forms. Metered-Dose Inhaler (MDI): (Budesonide/Formoterol) 80 mcg/4.5 mcg/inhalation, 160 mcg/4.5 mcg/inhalation

Common FDA Label Indication, Dosing, and Titration.

1. Asthma: Children ≥12 y of age and Adults, 80 mcg/4.5 mcg, 2 inhalations bid, may titrate to 160 mcg/4.5 mcg, 2 inhalations bid
2. COPD: 160 mcg/4.5 mcg 2 inhalations bid

Off-Label Uses.

1. Asthma: Children 5-11 y of age, 80 mcg/4.5 mcg, 2 inhalations bid

MOA. Budesonide is an anti-inflammatory with potent glucocorticoid and weak mineralocorticoid activity. It exhibits a broad range of active inhibition against multiple cell types and mediators involving allergic and nonallergic/irritant-mediated inflammation. Formoterol is a long-acting selective β_2-adrenergic agonist that produces bronchodilation.

80 mcg/4.5 mcg 160 mcg/4.5 mcg
AstraZeneca pictured

Drug Characteristics: Budesonide/Formoterol

Dose Adjustment Hepatic	Not required	**Absorption**	F = 39% for budesonide; unknown for formoterol inhalation
Dose Adjustment Renal	Not required	**Distribution**	Protein binding 85-90% (budesonide); 31-64% for formoterol
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP3A4/5 (budesonide)
Pregnancy Category	C	**Elimination**	Renal elimination is 60% with a half-life of 2-3 h (budesonide); renal elimination is 1-28% with a half-life of 10 h (formoterol)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to budesonide or formoterol; primary treatment of status asthmaticus or acute episodes of asthma or COPD	**Black Box Warnings**	Asthma deaths; pediatrics, increased risk of hospitalization

Medication Safety Issues: Budesonide/Formoterol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Budesonide/Formoterol

Typical Agents	Mechanism	Clinical Management
Short-acting sympathomimetics	May potentiate formoterol effect	Avoid concurrent use
Beta-blockers	May decrease effectiveness of formoterol and produce bronchospasms	Avoid use of nonselective beta-blocker in patients with COPD. Monitor PFTs if cardioselective beta-blockers clinically indicated
MAOI and tricyclic antidepressants	May potentiate formoterol effect on cardiovascular system	Consider alternative therapy
Azole antifungals and macrolides	Increased budesonide concentrations	Avoid long-term concomitant therapy with budesonide
CYP3A4/5 inducers	Increased budesonide metabolism reduces budesonide effectiveness	Monitor and consider dose increases of budesonide
CYP3A4/5 inhibitors	Decreased budesonide metabolism increases risk of budesonide toxicity	Monitor and consider dose decreases of budesonide

Adverse Reactions: Budesonide/Formoterol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Upper respiratory tract infections	Cough, decrease in bone mineral density, dysphonia, headache, tremor, nasopharyngitis, nervousness, oral candidiasis, pain in throat	Asthma-related death, bronchospasm, hypokalemia, arrhythmias

Efficacy Monitoring Parameters. Monitor PFTs. Resolution of asthma symptoms (symptoms, number of exacerbations, nighttime awakenings, need for rescue albuterol).

Toxicity Monitoring Parameters. Growth velocity in pediatric patients during prolonged therapy; use alternative therapy or seek emergency treatment if paradoxical bronchospasms occur.

Key Patient Counseling Points. Advise patient on proper inhalation technique. If more than 1 inhalation is prescribed, wait 1 min after initial inhalation and shake the inhaler again before the next inhalation. After administration, rinse mouth with water and spit, and wash face to minimize risk of developing oral candidiasis. Wash the mouthpiece and air-dry thoroughly at least once a week.

Clinical Pearls. Long-acting beta-agonists (LABAs) increase the risk of asthma-related deaths. Budesonide/formoterol should only be used for patients not adequately controlled on a long-term asthma control medication. This drug is not indicated for acute asthma exacerbations. LABAs may increase the risk of asthma-related hospitalization in pediatric and adolescent patients.

BUPRENORPHINE/NALOXONE: Bunavail, Suboxone, Zubsolv, Various

Class: Opioid Partial Agonist and Antagonist Combination. C-III

Dosage Forms. Sublingual Film: (Buprenorphine/Naloxone) 2 mg/0.5 mg, 8 mg/2 mg; **Sublingual Tablet:** (Buprenorphine/Naloxone) 1.4 mg/0.36 mg, 2 mg/0.5 mg, 5.7 mg/1.4mg, 8 mg/2 mg; **Buccal Film:** (Buprenorphine/Naloxone) 2.1 mg/0.3 mg, 4.2 mg/0.7 mg, 6.3 mg/1 mg

Reckitt Benckiser 8 mg/2 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Opioid dependence: Adults and children >16 y of age, 12-16 mg (buprenorphine component) once daily sublingually, titrate to response; typical dose range from 4 to 24 mg/d

Off-Label Uses. None

MOA. Buprenorphine is a μ-opioid receptor partial agonist and a κ-opioid receptor antagonist. Naloxone is a μ-opioid receptor antagonist that causes opioid withdrawal when injected parenterally and is included in the formulation to reduce the risk of abuse.

Drug Characteristics: Buprenorphine/Naloxone

Dose Adjustment Hepatic	Use with caution	**Absorption**	F = 15% (buprenorphine); F = 3% (naloxone)
Dose Adjustment Renal	Not required	**Distribution**	Vd = 97-187 L (buprenorphine)
Dialyzable	Unknown	**Metabolism**	Buprenorphine, hepatic, major substrate of CYP3A4/5; naloxone: hepatic via glucuronidation
Pregnancy Category	C	**Elimination**	30% renal elimination with half-life of 33 h (buprenorphine); half-life of 6 h (naloxone)
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Buprenorphine/Naloxone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes, medication guide required	No	No

Drug Interactions: Buprenorphine/Naloxone

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP3A4/5 inducers	Increased buprenorphine metabolism reduces buprenorphine effectiveness	Monitor and consider dose increases of buprenorphine
CYP3A4/5 inhibitors	Decreased buprenorphine metabolism increases risk of buprenorphine toxicity	Monitor and consider dose decreases of buprenorphine

Adverse Reactions: Buprenorphine/Naloxone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Vasodilation, sweating, headaches, insomnia, constipation, GI distress, opioid withdrawal, dizziness	Dyspnea, respiratory depression, glossodynia	Stevens-Johnson syndrome, physical dependence, tolerance, elevated liver functions tests, seizures

Efficacy Monitoring Parameters. Urine drug screening tests that are negative for illicit drugs. Relief of signs and symptoms associated with narcotic addiction.

Toxicity Monitoring Parameters. Severe skin rash, excessive drowsiness, decreased breathing, severe constipation.

Key Patient Counseling Points. Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Do not crush or swallow the sublingual tablet. Place the tablet under the tongue until it is dissolved. If you take 2 or more tablets at a time, place all of the tablets under the tongue together. If this is uncomfortable, place 2 tablets at a time under the tongue and repeat the process until all tablets have been taken. If you are using the sublingual film, place the film under the tongue until it is dissolved. If you need to take an additional film, place the new film on the opposite side from the first film. Do not chew, swallow, or move the film after placing it under the tongue. If using the buccal film, press and hold film to moistened cheek for 5 s with finger. If you need an additional film, place on the inside of other cheek. Do not use more than 2 buccal films simultaneously.

Clinical Pearls. Taking opioids will result in precipitation of withdrawal symptoms. The opioid agonist properties of buprenorphine are limited by a ceiling effect which occurs at higher doses. The strength of sublingual films and tablets are not interchangeable. For example, one 8 mg film is not equivalent to 4 films of 2 mg each. Do not substitute multiple smaller dose films to equal a larger dose. Recommended as a component of therapy including counseling and psychosocial support. Not recommended for treatment of dependence on long-acting opiates or methadone; useful for withdrawal of short-acting opiates and heroin.

BUPROPION: Wellbutrin, Zyban, Various

Class: Monocyclic Antidepressant

Dosage Forms. Oral Tablet (Immediate Release): 75 mg, 100 mg; **Oral Tablet (Sustained Release 12 h):** 100 mg, 150 mg, 200 mg; **Oral Tablet (Hydrochloride, Extended Release 24 h):** 150 mg, 300 mg, 450 mg; **Oral Tablet (Hydrobromide. Extended Release 24 h):** 174 mg, 348 mg, 522 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Immediate release, 100 mg po bid × 3 d, increase to 100 mg po tid (*max* 450 mg/d); Sustained release, 150 mg po daily in the morning × 3 d, then increase to 150 mg po bid (*max* 200 mg bid); Extended release, 150 mg po daily × 3 d, then increase to 300 mg po daily (*max* 450 mg/d)
2. Seasonal affective disorder (SAD): 150 or 174 mg once daily in the morning, may titrate to 300 or 348 mg once daily in the morning
3. Smoking cessation assistance: Sustained release, 150 mg po daily in the morning × 3 d, then 150 mg po bid (*max* 300 mg/d) for 7-12 wk; begin treatment 1 wk prior to smoking quit date

Off-Label Uses. None

MOA. Bupropion is a monocyclic antidepressant, unique as a mild dopamine and norepinephrine uptake inhibitor with no direct effect on serotonin receptors or MAO.

Drug Characteristics: Bupropion

Dose Adjustment Hepatic	Mild to moderate: reduce frequency and/or dose. Severe liver disease: *max* dose 75 mg daily	**Absorption**	Food has minimal effect on absorption
Dose Adjustment Renal	Reduce frequency and/or dose	**Distribution**	Vd = 19-21 L/kg; 84% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, 10-15%; major substrate of CYP2B6; inhibitor of CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 87% and 10% in feces, with a half-life of 14-37 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Seizure disorder; history of anorexia/bulimia; use of MAOI within 14 d; patients undergoing abrupt discontinuation of ethanol, benzodiazepines, barbiturates, or antiepileptics	**Black Box Warnings**	Suicidality

Medication Safety Issues: Bupropion

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
SR and XL	BuPROPion	SR and XL formulations	No	BusPIRone	No

Drug Interactions: Bupropion

Typical Agents	Mechanism	Clinical Management
Alcohol	Increased risk of seizures	Avoid concomitant use
CYP3A4/5 inducers	Increased bupropion metabolism reduces bupropion effectiveness	Monitor and consider dose increases of bupropion
CYP3A4/5 inhibitors	Decreased bupropion metabolism increases risk of bupropion toxicity	Monitor and consider dose decreases of bupropion
CYP2D6 substrates	Decreased metabolism or activation of prodrugs requiring CYP2D6	Avoid concurrent use if substrate is narrow therapeutic index, otherwise consider dose modification

Adverse Reactions: Bupropion

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Agitation, constipation, dizziness, headache, insomnia, nausea, tachyarrhythmia, tremor, xerostomia	Anxiety, arthralgia, confusion, hostile behavior, hypertension, myalgia, pruritus, rash, urticaria	Cardiac dysrhythmia, mania, seizure, suicidal thoughts, wide QRS complex

Efficacy Monitoring Parameters. Improvement in depressive symptoms, may require 4-6 wk. Abstinence from tobacco products.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. BP and heart rate in patients using concomitant nicotine replacement therapy.

Key Patient Counseling Points. Avoid alcohol, CNS depressants, and activities requiring mental alertness. Take at the same time each day and at bedtime if possible. If taking the extended-release tablet, the tablet shell may remain intact and be visible in the stool.

Clinical Pearls. Not FDA approved for use in children. Depression, suicidal ideation, attempts, and suicides occur in patients with and without preexisting psychiatric disease. When switching patients from immediate- or sustained-release tablets to extended-release tablets, give the same total daily dose when possible. Medication safety guide required.

BUSPIRONE: BuSpar, Various

Class: Antianxiety

Dosage Forms. Oral Tablet: 5 mg, 7.5 mg, 10 mg, 15 mg, 30 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Anxiety: Adults, 5 mg po bid-tid or 7.5 mg po bid, may titrate to 20-30 mg/d in 2-3 divided doses (*max* 60 mg/d)

Off-Label Uses.

1. Anxiety: Children, 5 mg/d po, may titrate to 15 mg po bid (*max* 50 mg/d)
2. Depression: Adults, 5 mg po tid, may titrate to 40-55 mg/d in 2-3 divided doses (*max* 90 mg/d)

MOA. Buspirone is the first of a class of selective serotonin-5-HT_{1A} receptor partial agonists. It also has some effect on dopamine-D_2 auto-receptors and, like antidepressants, can down-regulate β-adrenergic receptors. Unlike benzodiazepines, it lacks amnestic, anticonvulsant, muscle relaxant, and hypnotic effects. Its exact anxiolytic mechanism of action is complex and not clearly defined.

Drug Characteristics: Buspirone

Dose Adjustment Hepatic	Use lower initial doses and increase gradually as needed and tolerated	**Absorption**	F = 90%; food increases AUC and Cmax
Dose Adjustment Renal	Use lower initial doses and increase gradually as needed and tolerated	**Distribution**	Vd = 5.3 L/kg; 86% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP3A4/5
Pregnancy Category	B	**Elimination**	Renal elimination is 29-63% (primarily as metabolites), with a half-life of 2-3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Buspirone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	BusPIRone	No	No	BuPROPion	No

Drug Interactions: Buspirone

Typical Agents	Mechanism	Clinical Management
Linezolid, SSRIs, St. John's wort	Increased risk of serotonin syndrome	Monitor for symptoms (hypertension, hyperthermia, myoclonus, mental status changes)
CYP3A4/5 inducers	Increased buspirone metabolism reduces buspirone effectiveness	Monitor and consider dose increases of buspirone
CYP3A4/5 inhibitors	Decreased buspirone metabolism increases risk of buspirone toxicity	Monitor and consider dose decreases of buspirone

Adverse Reactions: Buspirone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness	Asthenia, confusion, diarrhea, excitement, feeling nervous, fatigue, headache, hostile behavior, nausea	Mania, psychiatric disorder

Efficacy Monitoring Parameters. Reduction in symptoms of anxiety.

Toxicity Monitoring Parameters. Signs and symptoms of withdrawal upon abrupt dose reduction or discontinuation.

Key Patient Counseling Points. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient that symptomatic improvement may not be seen for a few weeks. Advise patient against sudden discontinuation of drug. Patient may take with or without food, but should always take drug consistently. Patient should not drink alcohol or large amounts of grapefruit juice while taking this drug. Avoid concomitant use with MAOI.

Clinical Pearls. Safety and efficacy not established in pediatric patients <18 y of age.

CANDESARTAN: Atacand, Various

Class: Angiotensin II Receptor Antagonist

Dosage Forms. Oral Tablet: 4 mg, 8 mg, 16 mg, and 32 mg

AstraZeneca pictured

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: 4 mg po daily, may titrate to 32 mg/d po
2. Hypertension: Adults, 16 mg po daily or in 2 divided doses, may titrate to 32 mg po daily; Children 1-5 y of age, 0.2 mg/kg po daily, may titrate to 0.4 mg/kg daily; Children 6-16 y of age and <50 kg, 4-8 mg po daily, may titrate to 32 mg daily; Children 6-16 y of age and ≥50 kg, 8-16 mg po daily, may titrate to 32 mg daily

Off-Label Uses. None

MOA. Candesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor type 1 (AT1).

Drug Characteristics: Candesartan

Dose Adjustment Hepatic	Decrease dose in patients with moderate hepatic impairment	**Absorption**	F = 15%, food does not affect absorption
Dose Adjustment Renal	CrCl 15-60 mL/min, 8 mg po daily	**Distribution**	Vd = 0.13 L; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Parent compound bioactivated during absorption via ester hydrolysis within intestinal wall to candesartan
Pregnancy Category	D	**Elimination**	Renal elimination is 33% and fecal elimination is 67% with a half-life of 5-10 h (metabolite)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to candesartan or other ARB, pregnancy	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Candesartan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Antacid	No

Drug Interactions: Candesartan

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Eplerenone	Increased risk of hyperkalemia	Avoid concurrent use or monitor serum potassium levels
Potassium supplements	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive and natriuretic effect of candesartan, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP

Adverse Reactions: Candesartan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypotension	Back pain, constipation, dizziness, dyspepsia, f ushing, hyperkalemia, nephrotoxicity, tachycardia	Angioedema, birth defects, hepatotoxicity, rhabdomyolysis

Efficacy Monitoring Parameters. Decreased BP, resolution of heart failure; may require 3-6 wk to obtain therapeutic response.

Toxicity Monitoring Parameters. Report signs/symptoms of hypotension, tachycardia. Baseline and periodic sodium, potassium, total bicarbonate, BUN, SCr, and urinalysis prior to initiating therapy.

Key Patient Counseling Points. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek care if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs.

Clinical Pearls. Not indicated for use in children <1 y of age. Observe volume-depleted patient for hypotension with first dose. May cause progressive renal impairment and acute renal failure; those with preexisting renal impairment, heart failure, or diabetes are at increased risk.

CARBAMAZEPINE: Tegretol, Various

Class: Anticonvulsant

Dosage Forms. **Oral Tablet:** 200 mg; **Tablet, Chewable:** 100 mg; **Oral Tablet, Extended Release:** 100 mg, 200 mg, 400 mg; **Oral Suspension:** 100 mg/5 mL; **Oral Capsule, Extended Release:** 100 mg, 200 mg, 300 mg

Taro generic 200 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disease, acute manic and mixed episodes: 200 mg po bid, may titrate to 1600 mg/d po
2. Epilepsy, partial, generalized, and mixed types: Adults, 200 mg po bid, may titrate to 1200 mg po daily; Children <6 y of age, 10-20 mg/kg/d po in 2-3 divided doses, may titrate to 250-350 mg/d po; Children 6-12 y of age, 100 mg po bid, may titrate to 800 mg po daily
3. Trigeminal neuralgia: Regular release, 100 mg po q12h, may titrate to 1200 mg po daily prn for pain control

Off-Label Uses.

1. Neuropathic pain: 50-100 mg po bid in combination with opioids, may titrate to 1200 mg/d po

MOA. Carbamazepine acts presynaptically to block firing of action potentials, which decreases the release of excitatory neurotransmitters, and postsynaptically by blocking high-frequency repetitive discharge initiated at cell bodies.

Drug Characteristics: Carbamazepine

Dose Adjustment Hepatic	Avoid	**Absorption**	F = 89%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.59-2 L/kg; 75-90% protein bound
Dialyzable	Yes	**Metabolism**	Hepatic; major substrate of CYP3A4/5; strong inducer of CYP1A2, 2B6, 2C19, 2C8, 2C9, 3A4/5 and P-glycoprotein
Pregnancy Category	D	**Elimination**	Renal elimination 72%, with an initial half-life of 25-65 h, then 12-17 h after 3-5 wk due to autoinduction
Lactation	Compatible	**Pharmacogenetics**	Serious and sometimes fatal dermatologic reactions are more likely in patients with the inherited allelic variant HLA-B*1502. Avoid in individuals with this genotype
Contraindications	Hypersensitivity to carbamazepine, history of bone marrow depression, MAOIs, nefazodone	**Black Box Warnings**	Agranulocytosis; aplastic anemia; dermatological reactions (especially in Asians); screen for HLA-B*1502

Medication Safety Issues: Carbamazepine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	CarBAMazepine, TEGretol	Do not crush or chew ER tablets or capsules	No	OXcarbazepine, Toradol	No

Drug Interactions: Carbamazepine

Typical Agents	Mechanism	Clinical Management
Acetaminophen	Increased risk of hepatotoxicity	Monitor LFTs
CYP3A4/5 inducers	Increased carbamazepine metabolism reduces carbamazepine effectiveness	Monitor and consider dose increases of carbamazepine
CYP3A4/5 inhibitors	Decreased carbamazepine metabolism increases risk of carbamazepine toxicity	Monitor and consider dose decreases of carbamazepine
CYP1A2, 2B6, 2C19, 2C8, 2C9, 3A4/5 and P-glycoprotein substrates	Carbamazepine increases metabolism of substrates drugs, lowers plasma concentration, and decreases substrate drug activity	Avoid concurrent use, or monitor substrate drug and consider dose increase
Ergocalciferol	Increased catabolism of vitamin D	Monitor vitamin D levels and supplement
Diuretics	Increased risk of hyponatremia	Monitor electrolytes
MAOIs	Increased risk or ergotism	Contraindicated
Nefazodone	Inhibition of carbamazepine metabolism, induction of nefazodone metabolism	Contraindicated
Warfarin	Decreased anticoagulant effectiveness	Monitor INR

Adverse Reactions: Carbamazepine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hyponatremia	Blurred vision, confusion, hypocalcaemia, nausea, nystagmus, somnolence	Cardiac dysrhythmia, hepatitis, nephrotoxicity, pancreatitis, pancytopenia, Stevens-Johnson syndrome, syncope, toxic epidermal necrolysis

Efficacy Monitoring Parameters. Reduction in number of seizures, decreased pain, therapeutic concentrations for epilepsy: 4-12 mcg/mL.

Toxicity Monitoring Parameters. Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior; baseline CBC, serum sodium, LFTs, complete urinalysis, and BUN; thyroid function test at baseline and during therapy, eye examinations at baseline and during therapy.

Key Patient Counseling Points. May decrease effectiveness of oral contraceptives; use an alternative form of birth control. Avoid activities requiring mental alertness or coordination until drug effects are realized. Take with food, but not alcohol, grapefruit, or grapefruit juice. Avoid abrupt discontinuation.

Clinical Pearls. Carbamazepine is a drug of first choice for seizure disorder due to equivalent activity and decreased toxicity compared to other anti-seizure medications. Suspension is dosed 3-4 times per day.

CARBIDOPA/LEVODOPA: Sinemet, Various

Class: Antiparkinsonian

Dosage Forms. **Oral Tablet, Immediate Release:** (Carbidopa/Levodopa) 10 mg/100 mg, 25 mg/100 mg, 25 mg/250 mg; **Oral Tablet, Extended Release:** (Carbidopa/Levodopa) 25 mg/100 mg, 50 mg/200 mg; **Orally Disintegrating Tablet:** (Carbidopa/Levodopa) 10 mg/100 mg, 25 mg/100 mg, 25 mg/250 mg

25 mg/100 mg

25 mg/250 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Parkinson disease: Immediate release, 25 mg/100 mg po tid, increasing dose to therapeutic response; Extended release, 50 mg/200 mg po bid, separate doses by at least 6 h; patients generally treated with 400-1600 mg of levodopa per day; *max* 200 mg of carbidopa and 2000 mg of levodopa

Off-Label Uses.

1. Restless legs syndrome: 25 mg/100 mg po qhs, may repeat dose if awakening within 2 h

MOA. When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the CNS. For this reason, when given alone, large doses of levodopa are required for adequate therapeutic effect. However, these doses often result in nausea and other adverse reactions. Carbidopa inhibits decarboxylation of circulating levodopa, preventing nausea and allowing more levodopa to reach the CNS. Carbidopa does not cross the blood-brain barrier and does not affect the metabolism of levodopa within the CNS.

Drug Characteristics: Carbidopa/Levodopa

Dose Adjustment Hepatic	Not required	**Absorption**	Carbidopa F = 60%; levodopa F = 70-75%
Dose Adjustment Renal	Not required	**Distribution**	CSF concentrations of levodopa are 10-20% of plasma levels
Dialyzable	Not dialyzable	**Metabolism**	Levodopa undergoes extensive decarboxylation to dopamine in the gut wall, liver, and kidney; when given with carbidopa, peripheral decarboxylation of levodopa is blocked, increasing availability of levodopa for brain transport
Pregnancy Category	C	**Elimination**	Carbidopa renal elimination is 30% with a half-life of 1-2 h; levodopa renal elimination is 70-80% with a half-life of 45-90 min
Lactation	Avoid; may inhibit lactation	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to carbidopa or levodopa, narrow-angle glaucoma	**Black Box Warnings**	None

Medication Safety Issues: Carbidopa/Levodopa

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CR	No	Do not crush CR or oral disintegrating products	No	Serevent	No

Drug Interactions: Carbidopa/Levodopa

Typical Agents	Mechanism	Clinical Management
Dopamine D_2 receptor antagonists (isoniazid)	Reduction in therapeutic effect of levodopa	Increase dose of carbidopa/levodopa
Linezolid	Unknown; serotonin toxicity with severe hypertension	Concurrent use contraindicated; must wait at least 2 wk after discontinuing linezolid before initiating carbidopa/levodopa
MAOIs	Severe hypertension	Concurrent use contraindicated; must wait at least 2 wk after discontinuing MAOI before initiating carbidopa/levodopa
Phenytoin	Phenytoin reverses the effects of levodopa in Parkinson disease	Increase dose of carbidopa/levodopa

Adverse Reactions: Carbidopa/Levodopa

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dyskinesia	Nausea	Orthostatic hypotension, neuroleptic malignant syndrome

Efficacy Monitoring Parameters. Reduction in symptoms of Parkinson disease (extrapyramidal movements, rigidity, tremor, gait disturbances).

Toxicity Monitoring Parameters. Seek medical attention if GI bleeding and dyskinesia occur; monitor IOP in glaucoma patients who take this product.

Key Patient Counseling Points. Patients using concomitant antihypertensive may be at increased risk for postural hypotension. If you are using the oral disintegrating tabs, place on top of the tongue; does not require water or swallowing.

Clinical Pearls. Since levodopa competes with certain amino acids for transport across the gut wall, the absorption of levodopa may be impaired in some patients on a high protein diet. Parkinson disease is a progressive, neurodegenerative disorder of the extrapyramidal nervous system affecting the mobility and control of the skeletal muscular system. Its characteristic features include resting tremor, rigidity, and bradykinetic movements. Similar symptoms can occur (known as “parkinsonism”) due to manganese or carbon monoxide intoxication, after encephalitic conditions, and idiopathically. All are treated with levodopa/carbidopa at the same doses as used for Parkinson disease.

CARISOPRODOL: Soma, Various

Class: Centrally Acting Skeletal Muscle Relaxant. C-IV

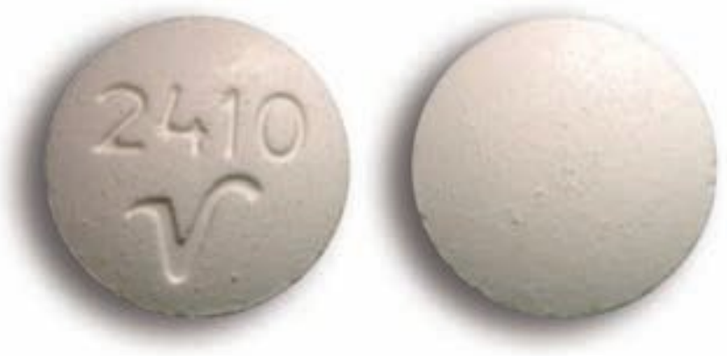
Dosage Forms. Oral Tablet: 250 mg, 350 mg

Common FDA Label Indication, Dosing, and Titration.

1. Disorder of musculoskeletal system: 250-350 mg po tid and hs

Off-Label Uses. None

MOA. Carisoprodol blocks interneuronal activity in descending reticular formation and spinal cord, resulting in muscle relaxation.



Qualitest generic 350 mg pictured

Drug Characteristics: Carisoprodol

Dose Adjustment Hepatic	Use lower doses initially and increase dose carefully in patients with hepatic failure	**Absorption**	Unknown
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Yes	**Metabolism**	Hepatic; major substrate of CYP2C19
Pregnancy Category	C	**Elimination**	Renal elimination is slight with a half-life of 8 h
Lactation	Avoid	**Pharmacogenetics**	CYP2C19 poor metabolizers at increased risk of toxicity
Contraindications	Hypersensitivity to carisoprodol or meprobamate, acute intermittent porphyria	**Black Box Warnings**	None

Medication Safety Issues: Carisoprodol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures.

Drug Interactions: Carisoprodol

Typical Agents	Mechanism	Clinical Management
CYP2C19 inducers	Increased carisoprodol metabolism reduces carisoprodol effectiveness	Monitor and consider dose increases of carisoprodol
CYP2C19 inhibitors	Decreased carisoprodol metabolism increases risk of carisoprodol toxicity	Monitor and consider dose decreases of carisoprodol
CNS depressants (opioids, benzodiazepines, alcohol)	Additive sedative effects	Avoid concurrent use or monitor carefully for signs of toxicity

Adverse Reactions: Carisoprodol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Drowsiness, dizziness	Headache	Seizure, drug dependence, withdrawal symptoms upon discontinuation after chronic use

Efficacy Monitoring Parameters. Reduction in pain and muscle spasms.

Toxicity Monitoring Parameters. Seek medical attention if idiosyncratic symptoms such as extreme weakness, transient quadriplegia, dizziness, confusion occur within minutes or hours after first dose.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Patients withdrawing from prolonged therapy should be monitored carefully for withdrawal symptoms, including seizures.

Clinical Pearls. Carisoprodol is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). The drug was approved by the FDA in 1959 and limited pharmacologic and pharmacokinetic data are available.

CARVEDILOL: Coreg, Coreg CR, Various

Class: α/β-Adrenergic Blocker

Dosage Forms. Oral Tablet: 3.125 mg, 6.25 mg, 12.5 mg, 25 mg; **Oral Capsule, Extended Release:** 10 mg, 20 mg, 40 mg, 80 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: Tablets, 3.125 mg po bid, *max* 25 mg po bid for patients weighing <85 kg, 50 mg po bid for patients weighing >85 kg; Extended-release capsule, 10 mg po daily in the morning, *max* 80 mg po daily
2. Hypertension: Tablet, 6.25 mg po bid; *max* 25 mg po bid; Extended-release capsule, 20 mg po daily in the morning, *max* 80 mg po daily
3. Impaired left ventricular function, myocardial infarction: Tablet, 3.125-6.25 mg po bid, may titrate to 25 mg po bid; Extended-release capsule, 10-20 mg po daily in the morning, *max* 80 mg po daily

Off-Label Uses.

1. Angina pectoris: 25-50 mg po bid
2. Cardiac dysrhythmia: 6.25 mg po bid, may titrate to 50 mg po bid

MOA. Carvedilol is a selective α_1- and nonselective β-adrenergic blocker that decreases AV nodal conduction in supraventricular tachycardias and blockade of catecholamine-induced dysrhythmias.

Drug Characteristics: Carvedilol

Dose Adjustment Hepatic	Avoid use in patients with hepatic impairment; contraindicated in severe liver dysfunction	**Absorption**	F = 25-35%; food significantly increases AUC and Cmax for extended-release product
Dose Adjustment Renal	Not required	**Distribution**	Vd = 115 L; >95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic 98%; major substrate of CYP2D6, P-glycoprotein; inhibitor of P-glycoprotein
Pregnancy Category	C	**Elimination**	Renal elimination is 16% and 60% in feces, with a half-life of 6-10 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 poor metabolizers with higher plasma levels, consider lower initial dose
Contraindications	Hypersensitivity, bronchial asthma, severe sinus bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome, overt heart failure, cardiogenic shock, severe hepatic impairment	**Black Box Warnings**	None

Medication Safety Issues: Carvedilol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CR	No	No	No	Corgard, Cortef, Cozaar	No

Drug Interactions: Carvedilol

Typical Agents	Mechanism	Clinical Management
Calcium channel blockers, quinidine, amiodarone, dronedarone	Increased risk of bradycardia, atrioventricular block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
P-glycoprotein inducers	Increased carvedilol metabolism reduces carvedilol effectiveness	Monitor and consider dose increases of carvedilol
CYP2D6, P-glycoprotein inhibitors	Decreased carvedilol metabolism increases risk of carvedilol toxicity	Monitor and consider dose decreases of carvedilol
P-glycoprotein substrates	Carvedilol inhibits metabolism of substrates resulting in increased risk of substrate toxicity	Monitor and consider dose decreases of substrates
Insulin, oral hypoglycemic agents	May enhance the hypoglycemic effect of sulfonylureas, may also mask hypoglycemia	Monitor blood glucose levels
NSAIDs	Decreased antihypertensive effect of carvedilol	Avoid concurrent use or monitor BP

Adverse Reactions: Carvedilol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Cold extremities, dizziness, erectile dysfunction, fatigue, hypotension, weight gain	Arthralgia, bradyarrhythmias, bronchospasm, diarrhea, hyperglycemia, dyspnea, depression, headache, nausea, somnolence, syncope, vomiting	Heart failure, hepatotoxicity, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased HR, bronchospasm, increased blood glucose levels in diabetic patients, and hepatotoxicity.

Key Patient Counseling Points. Take carvedilol with food or milk. Report signs/symptoms of heart failure, bradyarrhythmias, bronchospasm, hepatotoxicity, hypotension, syncope, or exacerbation of angina with initial dosing and dose changes. Avoid alcohol. Avoid abrupt discontinuation, may cause rebound hypertension. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Diabetic patients carefully follow blood sugar levels as β-blockers may mask symptoms of hypoglycemia.

Clinical Pearls. Safety and efficacy not established in pediatric patients. Reduce dose with bradycardia (<55 beats/min).

CEFDINIR: Omnicef, Various

Class: Third-Generation Cephalosporin

Dosage Forms. **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Capsule:** 300 mg

Common FDA Label Indication, Dosing, and Titration.

1. Acute otitis media, pharyngitis, tonsillitis: Children 6 mo through 12 y, 7 mg/kg po bid × 5-10 d or 14 mg/kg po daily x 10 d; *max* 600 mg/d; Adults, 300 mg po bid × 5-10 d
2. Bronchitis, acute, secondary bacterial infection: Adults and Children >12 y of age, 300 mg po bid × 5-10 d
3. Community-acquired pneumonia, uncomplicated skin, and/or subcutaneous tissue infection: 300 mg po bid × 10 d

Off-Label Uses. None

MOA. Cefdinir is a third-generation cephalosporin with activity against a number of gram-positive and gram-negative bacteria including β-lactamase–producing strains.

Aurobindo generic 300 mg pictured

C

Drug Characteristics: Cefdinir

Dose Adjustment Hepatic	Not required	**Absorption**	F = 25%, food decreases absorption by 30%
Dose Adjustment Renal	CrCl <30 mL/min, decrease interval to daily	**Distribution**	Lung, maxillary sinus, middle ear fluid, skin, sputum
Dialyzable	Administer after hemodialysis and decrease interval to every other day	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 18% with a half-life of 2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cephalosporin	**Black Box Warnings**	None

Medication Safety Issues: Cefdinir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Cefdinir

Typical Agents	Mechanism	Clinical Management
Antacids, iron, vitamins	Decreased absorption	Separate administration by 2 h

Adverse Reactions: Cefdinir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea	Nausea and vomiting, vaginitis, headache	Increased liver enzymes, hypersensitivity

Efficacy Monitoring Parameters. Resolution of infection.

Toxicity Monitoring Parameters. Seek medical attention if severe diarrhea.

Key Patient Counseling Points. Complete full course of therapy. For the suspension, shake well and can be stored at room temperature. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Separate administration of antacids, iron, and vitamins by 2 h.

Clinical Pearls. May resume normal activities after 24 h of antibiotics and if afebrile. Approximately 10% of patients allergic to penicillin are also allergic to cephalosporin; use with caution in penicillin-allergic patients.

CEFUROXIME: Ceftin, Various

Class: Second-Generation Cephalosporin

Dosage Forms. **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Tablet:** 125 mg, 250 mg, 500 mg

Northstar Rx generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute infective exacerbation of COPD, uncomplicated skin and/or subcutaneous tissue infection, acute bacterial maxillary sinusitis, uncomplicated urinary tract infection: Adults, 250-500 mg po bid × 10 d
2. Acute otitis media: Children who are able to swallow tablets, 250 mg po bid × 10 d
3. Bronchitis, acute, secondary bacterial infection: Adults and Children >12 y of age, 250-500 mg po bid × 5-10 d
4. Gonorrhea, uncomplicated: 1 g po × 1 dose
5. Impetigo: Children 3 mo to 12 y of age, suspension 30 mg/kg/d po in 2 divided doses × 10 d, *max* 1 g/d
6. Lyme disease: 500 mg po bid × 14-21 d
7. Pharyngitis, tonsillitis: Adults: 250 mg po bid × 10 d; Children 3 mo to 12 y of age, suspension 20 mg/kg/d po in 2 divided doses for 10 d, *max* 500 mg/d

Off-Label Uses. None

MOA. Cefuroxime is a second-generation cephalosporin whose activity is better than cefazolin but less than cefotaxime, against *H. influenzae*, including β-lactamase–producing strains. The activity of cefuroxime against *S. aureus* is slightly less than that of cefazolin. Its activity against anaerobes is poor, similar to the first-generation cephalosporins.

Drug Characteristics: Cefuroxime

Dose Adjustment Hepatic	Not required	**Absorption**	F = 37%, food increases absorption to 52%, suspension must be taken with food; tablets can be taken without regard to food
Dose Adjustment Renal	CrCl = 10-30 mL/min, administer full dose every 24 h; CrCl ≤10 mL/min, administer full dose every 48 h	**Distribution**	Aqueous humor, bronchial secretions, ear fluid, placenta, sinus
Dialyzable	Dialyzable by both hemodialysis and peritoneal dialysis	**Metabolism**	Cefuroxime is rapidly hydrolyzed by plasma and GI esterases
Pregnancy Category	B	**Elimination**	Renal elimination is 50% with a half-life of 2 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cephalosporins	**Black Box Warnings**	None

Medication Safety Issues: Cefuroxime

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush or chew tablets due to persistent bitter taste	No	Cefzil, Cipro	No

Drug Interactions: Cefuroxime

Typical Agents	Mechanism	Clinical Management
Ethinyl estradiol and other estrogen-based birth control products	Alters intestinal flora which, in turn, reduces the enterohepatic circulation of estrogen metabolites; decreased efficacy of birth control	Use an alternative form of birth control

Adverse Reactions: Cefuroxime

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea	Nausea and vomiting, vaginitis, increased liver enzymes	Stevens-Johnson syndrome, hepatotoxicity, severe hypersensitivity, anemia, neutropenia, pancytopenia, seizure

Efficacy Monitoring Parameters. Resolution of infection.

Toxicity Monitoring Parameters. Yellowing of the eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath.

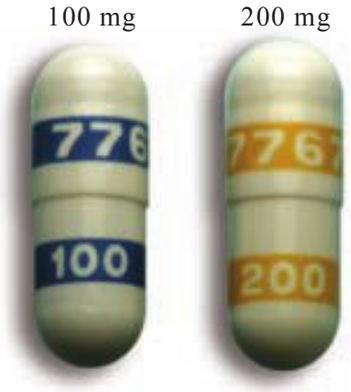
Key Patient Counseling Points. Seek medical attention if rash develops. Complete full course of therapy. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

Clinical Pearls. May resume normal activities after 24 h of antibiotics if afebrile. Approximately 10% of patients allergic to penicillins are also allergic to cephalosporins; use with caution in penicillin-allergic patients. Dosing of suspension and tablets are not interchangeable. Also available in injectable formulation.

CELECOXIB: Celebrex

Class: Cyclooxygenase-2 Inhibitor

Dosage Forms. Oral Capsule: 50 mg, 100 mg, 200 mg, 400 mg



Pfizer pictured

Common FDA Label Indication and Dosing.

1. Osteoarthritis: 100 mg po bid or 200 mg po daily
2. Rheumatoid arthritis: Adults, 100-200 mg po bid; Children >2 y of age, 10-25 kg, 50 mg po bid, >25 kg, 100 mg po bid
3. Ankylosing spondylitis: 100 mg po bid
4. Acute pain, primary dysmenorrhea: 200 mg po bid prn

Off-Label Uses.

1. Gout: 400 mg po bid × 7 d

MOA. Inhibition of the COX-2 enzyme isoform is thought to be responsible for the anti-inflammatory effects of NSAIDs, whereas inhibition of COX-1 results in GI and possibly other side effects.

Drug Characteristics: Celecoxib

Dose Adjustment Hepatic	Moderate: reduce dose by 50%; severe: avoid use	**Absorption**	Well absorbed, food enhances absorption
Dose Adjustment Renal	CrCl <30 mL/min: avoid use	**Distribution**	Vd = 400 L; 97% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic 97%; major substrate of CYP2C9; moderate inhibitor of CYP2C8 and 2D6
Pregnancy Category	D	**Elimination**	27% renal elimination with a half-life of 11 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Consider dose reduction of 50% in CYP2C9 poor metabolizers
Contraindications	Asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain, hypersensitivity to sulfonamides	**Black Box Warnings**	GI toxicity, cardiotoxicity, CABG

Medication Safety Issues: Celecoxib

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	CeleBREX	No	No	CeleXA, Cerebyx, Cervarix, Clarinex	No

Drug Interactions: Celecoxib

Typical Agents	Mechanism	Clinical Management
Aspirin, SSRIs	Additive GI toxicity	Monitor for GI toxicity
Angiotensin II receptor blockers, thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
CYP2C9 inducers	Increased celecoxib metabolism reduces celecoxib effectiveness	Monitor and consider dose increases of celecoxib
CYP2C9 inhibitors	Decreased celecoxib metabolism increases risk of celecoxib toxicity	Monitor and consider dose decreases of celecoxib
CYP2D6 and 2C8 substrates	Decreased metabolism and increased toxicity of substrates	Monitor and consider substrate dose reduction
Lithium	Increased lithium levels, unknown mechanism	Monitor lithium concentrations and adjust
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction
Warfarin	Both substrates for CYP2C9, competitive metabolism	Monitor INR and adjust warfarin dose

Adverse Reactions: Celecoxib

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypertension, headaches, GI distress, diarrhea	Myocardial infarction, bronchospasm	Stevens-Johnson syndrome, GI ulcers and bleeding, thrombosis, elevated liver functions, acute renal failure

Efficacy Monitoring Parameters. Decreased pain and improved range of motion, regression of colonic polyps on colonoscopy.

Toxicity Monitoring Parameters. CBC, LFTs, SCr, fecal occult blood tests, BP, severe skin rash, black tarry stools, swelling or weight gain, severe pain, yellowing of eyes of skin, change in urination.

Key Patient Counseling Points. Take with food or milk to decrease GI upset. May open capsule and pour into a teaspoon of applesauce.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk for cardiovascular effects. Celecoxib has less risk of GI effects than other NSAIDs, but increased cardiovascular toxicity.

CEPHALEXIN: Keflex, Various

Class: First-Generation Cephalosporin

Dosage Forms. **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Tablet:** 250 mg, 500 mg; **Oral Capsule:** 250 mg, 500 mg, 750 mg

Teva generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Infection of skin and/or subcutaneous tissue: Adults, 500 mg po q12h; Children, 25-50 mg/kg/d po divided q12h
2. Osteomyelitis: Adults, 250 mg-1 g po q6h; Children, 25-100 mg/kg/d po divided q6h, *max* 4 g/d
3. Otitis media, respiratory tract infection, urinary tract infection: Adults, 250 mg-1 g po q6h; Children, 25-100 mg/kg/d po divided q6h, *max* 4 g/d
4. Streptococcal pharyngitis: Adults, 500 mg po q12h × 10 d; Children, 25-50 mg/kg/d po divided q6h × 10 d, *max* 4 g/d

Off-Label Uses.

1. Bacterial endocarditis; prophylaxis for high-risk patients; dental, respiratory, or infected skin/skin structure or musculoskeletal tissue procedures: Adults, 2 g po 30-60 min prior to procedure; Children, 50 mg/kg 30-60 min prior to procedure

MOA. Cephalexin is a first-generation cephalosporin that inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). Most gram-positive bacteria, including non-penicillinase and penicillinase-producing staphylococci, and streptococci. Activity against gram-negative bacteria is less than that observed with the second- and third-generation cephalosporins and is primarily restricted to *E. coli*, *Klebsiella*, and *P. mirabilis*.

Drug Characteristics: Cephalexin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%, food has little effect on absorption
Dose Adjustment Renal	CrCl <50 mL/min, 500 mg q12h	**Distribution**	Bile, joints, placenta, sputum
Dialyzable	Dialyzable by both hemodialysis and peritoneal dialysis	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 69-100% with a half-life of 1 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cephalosporins	**Black Box Warnings**	None

Medication Safety Issues: Cephalexin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Cefaclor, ceFAZolin, ciprofloxacin, Valtrex	No

Drug Interactions: Cephalexin

Typical Agents	Mechanism	Clinical Management
Cholestyramine	Cholestyramine may bind to and decrease absorption of cephalexin	Administer cephalexin 1 h before or 6 h after cholestyramine
Metformin	Cephalexin may decrease metformin renal excretion leading to increased metformin toxicity	Use with caution; increase monitoring for metformin toxicity

Adverse Reactions: Cephalexin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea and vomiting	Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, seizure

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Seek medical attention if decreased urination, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath.

Key Patient Counseling Points. Seek medical attention if rash develops. Complete full course of therapy. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

Clinical Pearls. May resume normal activities after 24 h of antibiotics and if afebrile. Approximately 10% of patients allergic to penicillins are also allergic to cephalosporins; use with caution in penicillin-allergic patients.

CETIRIZINE: Zyrtec, Various

Class: Antihistamine

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet, Chewable:** 5 mg, 10 mg; **Oral Capsule:** 10 mg; **Oral Solution:** 1 mg/mL; **Oral Syrup:** 1 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Perennial or seasonal allergic rhinitis: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily
2. Urticaria, chronic: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily

Off-Label Uses.

1. Atopic dermatitis: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily

MOA. Cetirizine is a low-sedating, long-acting H_1-receptor antagonist that is a metabolite of hydroxyzine. Cetirizine competitively inhibits the interaction of histamine with H_1 receptors, thereby preventing the allergic response.

Drug Characteristics: Cetirizine

Dose Adjustment Hepatic	Chronic liver failure, 5 mg po daily	**Absorption**	F = 70%, limited effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, 5 mg po daily	**Distribution**	Vd = 0.5-0.8 L/kg with 90% protein binding
Dialyzable	Yes	**Metabolism**	Limited hepatic; substrate of P-glycoprotein
Pregnancy Category	B	**Elimination**	Renal elimination is 70% with a half-life of 8.3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cetirizine or hydroxyzine	**Black Box Warnings**	None

Sunmark 1 mg/mL generic solution pictured

Medication Safety Issues: Cetirizine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ZyrTEC-D	ZyrTEC	No	No	ZyrTEC Itchy Eye (ketotifen), Zantac	No

Drug Interactions: Cetirizine

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Possible increase in sedation effects	Use concurrently with caution
P-glycoprotein inducers	Increased cetirizine metabolism reduces cetirizine effectiveness	Monitor and consider dose increases of cetirizine
P-glycoprotein inhibitors	Decreased cetirizine metabolism increases risk of cetirizine toxicity	Monitor and consider dose decreases of cetirizine

Adverse Reactions: Cetirizine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Drowsiness	Sedation, headache, dry mouth, fatigue, and nausea	

Efficacy Monitoring Parameters. Improvement in rhinitis or urticaria symptoms.

Toxicity Monitoring Parameters. Seek medical attention for signs of severe CNS toxicity.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

Clinical Pearls. Product is available in several nonprescription dosage forms.

CHLORHEXIDINE: Peridex, Hibiclens, Various

Class: Antibacterial Cleansing Agent

Dosage Forms. **Liquid Oral Rinse:** 0.12%; **Topical Solution:** 2%, 4%

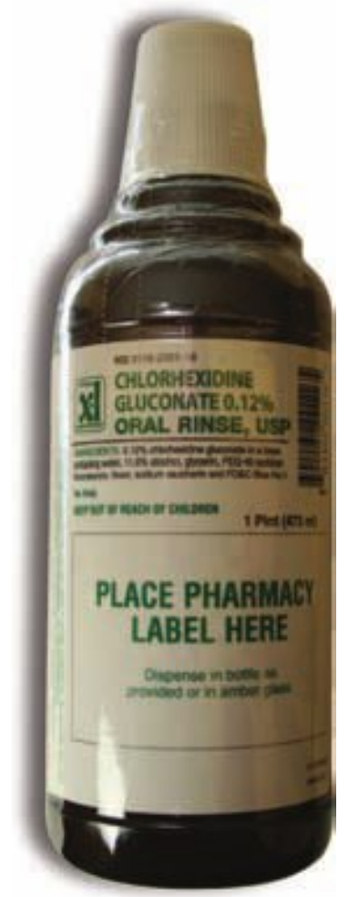
Common FDA Label Indication, Dosing, and Titration.

1. Gingivitis: 15 mL oral rinse (undiluted, 0.12%), swish 30 s and spit bid (morning and evening) after tooth brushing
2. Skin or wound cleansing: Rinse area to be cleansed, apply minimum amount of solution necessary to cover skin or wound area, and wash gently; then rinse

Off-Label Uses.

1. Burn, prevention of nosocomial infectious disease: Rinse area to be cleansed, apply minimum amount of 4% solution necessary to cover skin or wound area, and wash gently; then rinse
2. Oropharyngeal decontamination, to reduce risk of ventilator-associated pneumonia in critically ill patients: 15 mL oral rinse (undiluted, 0.12%), swab oral area q8h

MOA. Chlorhexidine, a polybiguanide, is an antiseptic and antimicrobial drug with bactericidal activity. The bactericidal effect of chlorhexidine is a result of the binding of this cationic molecule to negatively charged bacterial cell walls and extracellular microbial complexes.



Xttrium generic pictured

Drug Characteristics: Chlorhexidine

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to chlorhexidine	**Black Box Warnings**	None

Medication Safety Issues: Chlorhexidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Precedex	No

Drug Interactions: Chlorhexidine. None

Adverse Reactions: Chlorhexidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Tooth aches and discolored teeth with oral rinse	GI irritation	Allergic reactions, skin irritation

Efficacy Monitoring Parameters. Oral rinse: resolution of gingivitis. Topical: no signs of bacterial infection (redness, pruritus, burning, swelling).

Toxicity Monitoring Parameters. Tooth discoloration, skin irritation.

Key Patient Counseling Points. For oral rinse, measure out 1/2 fluid ounce (15 mL) as marked in the cap which comes with the bottle, swish the solution in mouth for at least 30 s; do not swallow. Wait several hours after use of chlorhexidine to eat or drink. Likely to cause tooth discoloration, which can be removed by dental cleaning. For topical product, use only on unbroken skin, do not swallow, or get in the eyes, ears, mouth, nose, genital area, or anal area. Contains large amounts of alcohol (70%) and are flammable. Apply the medicine in a well-ventilated place. Do not cover the treated area until the medicine is completely dry. This is usually 3 min or longer for hairless skin. If you must apply the medicine to a hairy area of the body, wipe the area with a towel to remove extra medicine.

Clinical Pearls. Not for use in children. Several nonprescription products also available.

CHLORTHALIDONE: Hygroton, Thalitone, Various

Class: Thiazide Diuretic

Dosage Forms. Oral Tablet: 25 mg, 50 mg, 100 mg

Mylan generic 25 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, 25 mg po daily, may titrate to *max* of 100 mg po daily
2. Edema: 50 mg po daily, may titrate to *max* of 200 mg po daily; heart failure–associated edema, 12.5-25 mg po daily, may titrate to *max* of 100 po daily

Off-Label Uses.

1. Hypertension: Children, 0.3 mg/kg po daily, may titrate to *max* of 2 mg/kg/d or 50 mg/d, whichever is less
2. Calcium nephrolithiasis, prevention of recurrent kidney stones: 25 mg po daily

MOA. Chlorthalidone increases sodium and chloride excretion by interfering with their reabsorption in the cortical-diluting segment of the nephron.

Drug Characteristics: Chlorthalidone

Dose Adjustment Hepatic	Not required	**Absorption**	F = 65%, food has no effect on absorption
Dose Adjustment Renal	CrCl <10 mL/min: increase dosing interval to q48h	**Distribution**	Vd = 3-13 L/kg; protein binding 75%
Dialyzable	Not dialyzable	**Metabolism**	Hepatic
Pregnancy Category	B	**Elimination**	Renal elimination 50-74%, half-life of 40-60 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to chlorthalidone or sulfonamides; anuria	**Black Box Warnings**	None

Medication Safety Issues: Chlorthalidone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Chlorthalidone

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of chlorthalidone	Avoid concurrent use or monitor BP
Calcium channel blockers, quinidine	Increased risk of hypotension and/or bradycardia and atrioventricular block	Avoid concurrent use
Digoxin	Increased risk of AV block	Monitor HR, ECG, and serum digoxin concentrations
ACE-Is	Increased risk of postural hypotension (first dose)	Start with low dose of ACE-I and monitor BP
Dofetilide	Increased risk of ventricular arrhythmias (torsades de pointes) due to hypokalemia, hypomagnesemia	Avoid concurrent use

Adverse Reactions: Chlorthalidone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, hypotension, hyperuricemia	Anorexia, diarrhea, headache, hypokalemia, hyponatremia, nausea, orthostatic hypotension, rash	Heart failure, pancreatitis

Efficacy Monitoring Parameters. Decreased BP, swelling, edema.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes, uric acid, and renal function at baseline and periodically.

Key Patient Counseling Points. Instruct patient to report signs/symptoms of dyspnea, hypotension, gout, or heart failure. Avoid alcohol and NSAIDs. Avoid abrupt discontinuation. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Instruct patient to rise slowly from sitting/supine position, as drug may cause orthostatic hypotension. Instruct patient to eat high-potassium foods during therapy.

Clinical Pearls. Chlorthalidone is not FDA approved for use in children, but it is included in guidelines and can be used off label.

CIPROFLOXACIN ORAL: Cipro, Cipro XR, Various

Class: Fluoroquinolone Antibiotic

Dosage Forms. **Microcapsules for Oral Suspension:** 250 mg/5 mL, 500 mg/5 mL; **Oral Tablet:** 100 mg, 250 mg, 500 mg, 750 mg; **Oral Tablet, Extended Release:** 500 mg, 1000 mg

Northstar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Anthrax, postexposure prophylaxis: Adults, 500 mg po q12h × at least 60 d, Children, 15 mg/kg po bid × at least 60 d, *max* 500 mg/dose
2. Bacterial prostatitis, chronic: 500 mg po q12h × 28 d
3. Bronchitis, lower respiratory tract infection, infection of bone, skin, or soft tissue, sinusitis: 500-750 mg po q12h × 7-14 d
4. Urinary tract infectious disease: 250-500 mg po q12h or 500 mg (extended release) q24h × 3 d

Off-Label Uses.

1. Chancroid: 500 mg po bid × 3 d
2. Traveler's diarrhea: 750 mg po as a single dose (mild); 500 mg po bid × 3 d (severe)

MOA: Ciprofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase. It is highly active against aerobic, gram-negative bacilli.

Drug Characteristics: Ciprofloxacin Oral

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60-80%, minor food effect
Dose Adjustment Renal	CrCl 30-50 mL/min, 250-500 mg q12h; CrCl 5-29 mL/min, 250-500 mg q18h	**Distribution**	Widespread (bile, CSF, gynecologic tissues, liver, lung, prostate, peritoneum, synovial fluid, sputum, etc)
Dialyzable	Dialyzable by both hemodialysis and peritoneal dialysis. Give 250-500 mg q24h after dialysis	**Metabolism**	Not metabolized; substrate of P-glycoprotein; strong inhibitor of CYP1A2
Pregnancy Category	C	**Elimination**	Renal elimination is 30-57% with a half-life of 3-6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Serious and sometimes fatal hemolytic reactions may occur in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency
Contraindications	Hypersensitivity to ciprofloxacin or other quinolones, concomitant tizanidine	**Black Box Warnings**	Myasthenia gravis, tendon inflammation and rupture

Medication Safety Issues: Ciprofloxacin Oral

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	No	Do not crush Cipro XR	No	Ceftin, cephalexin	No

Drug Interactions: Ciprof oxacin Oral

Typical Agents	Mechanism	Clinical Management
Diabetic agents	Hypoglycemic or hyperglycemic episodes, mechanism unknown	Avoid concurrent use; monitor FPG and consider dose adjustments of antidiabetic agent
Aluminum, calcium, and magnesium-containing antacids, calcium fortified foods, didanosine, iron, sevelamer	Decreased absorption of ciprof oxacin caused by chelation	Take ciprof oxacin 2 h before or 6 h after
Corticosteroids	Increased risk of tendon rupture	Counsel patients to discontinue ciprof oxacin and seek medical attention if tendon pain or rupture
CYP1A2 substrates	Ciprof oxacin inhibits CYP1A2 reducing substrate metabolism and increased substrate toxicity	Monitor for toxicity and consider dose reductions of substrates
Warfarin	Increased risk of bleeding	Increased monitoring of INR and warfarin adjustments
P-glycoprotein inducers	Increased ciprof oxacin metabolism reduces ciprof oxacin effectiveness	Monitor and consider dose increases of ciprof oxacin
P-glycoprotein inhibitors	Decreased ciprof oxacin metabolism increases risk of ciprof oxacin toxicity	Monitor and consider dose decreases of ciprof oxacin

Adverse Reactions: Ciprof oxacin Oral

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Tooth discoloration in infants	Nausea and vomiting, rash, myalgia, arthralgia, tendinitis, headache	Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac effects, liver failure, myasthenia gravis, tendon rupture, renal failure, psychosis, QT prolongation

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Baseline SCr. If obtained, levels should be between 0.5 and 5 mcg/mL.

Key Patient Counseling Points. Seek medical attention if decreased urination, yellowing of eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, tendon pain. Take with or without food, but not with milk or other dairy products. Take ciprofloxacin at least 2 h before or 6 h after antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc. If using the suspension, shake well before use; suspension may be stored at room temperature.

Clinical Pearls. Not approved in children <18 y of age except for anthrax and complicated UTIs. Requires medication guide when dispensed. Also available in injectable, otic, and ophthalmic formulations.

CIPROFLOXACIN OTIC: Cipro HC, Cetraxal, Various

Class: Fluoroquinolone Antibiotic

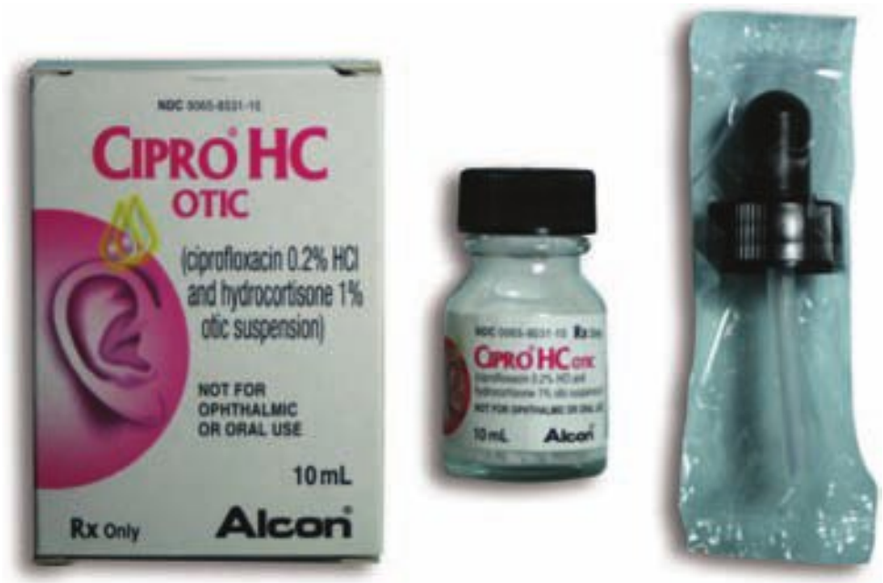
Dosage Forms. Otic Solution: 0.2%

Common FDA Label Indication, Dosing, and Titration.

1. Otitis externa, acute: Adults and Children >1 y of age, 0.25 mL (entire single-use container) into affected ear(s) bid (approximately q12h) × 7 d

Off-Label Uses. None

MOA. Ciprofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase, an enzyme responsible for the unwinding of DNA for transcription and subsequent supercoiling of DNA for packaging into chromosomal subunits. It is highly active against aerobic, gram-negative bacilli, especially Enterobacteriaceae, with MICs often <0.1 mg/L. It is also active against some strains of *P. aeruginosa* and *Staphylococcus* spp., with an MIC of 0.5-1 mg/L. However, recent reports indicate increasing resistance to this agent in *S. aureus*. It has poor activity against streptococci and anaerobes.



Alcon pictured

Drug Characteristics: Ciprofloxacin Otic

Dose Adjustment Hepatic	Not required	**Absorption**	Not systemically absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not systemically absorbed
Dialyzable	Not absorbed	**Metabolism**	Not systemically absorbed
Pregnancy Category	C	**Elimination**	Not systemically absorbed
Lactation	Unknown if ciprofloxacin otic solution is excreted into breast milk. Weigh risks and benefits	**Pharmacogenetics**	None known that affect otic solution administration
Contraindications	Hypersensitivity to ciprofloxacin or other quinolones	**Black Box Warnings**	None

Medication Safety Issues: Ciprofloxacin Otic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	CefTRIAXone, cephalexin	No

Drug Interactions: Ciprofloxacin Otic. None known

Adverse Reactions: Ciprof oxacin Otic

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Application site pain and itching, fungal ear superinfection	Hypersensitivity reactions

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection. Cultures may be required if infection does not improve within 1 wk of therapy.

Toxicity Monitoring Parameters. Ear pain, local hypersensitivity reaction, secondary fungal infections.

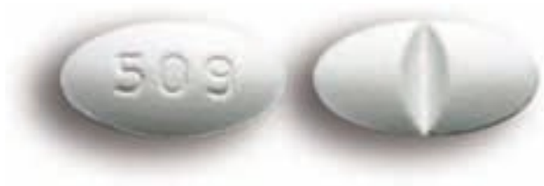
Key Patient Counseling Points. Warm solution by holding container in hands for at least 1 min before administering. Patient should lie with affected ear upward; position should be maintained for at least 1 min after instillation; repeat in the opposite ear if necessary.

Clinical Pearls. Ciprofloxacin otic is not approved in children <1 y of age. Not for ophthalmologic use, otic use only. Also available as injectable, ophthalmic, and oral formulations.

CITALOPRAM: Celexa, Various

Class: SSRI Antidepressant

Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg; **Oral Solution:** 10 mg/5 mL



Sun Pharmaceuticals generic 40 mg pictured

Greenstone generic 20 mg pictured

Blu Pharmaceuticals generic 10 mg pictured

C

Common FDA Label Indication, Dosing, and Titration.

1. Depression: 20 mg po daily, may titrate to 40 mg po daily

Off-Label Uses.

1. OCD: 20 mg po daily, may titrate to 40 mg/d
2. Panic disorder: 20-30 mg po daily, may titrate to 40 mg po daily

MOA. Citalopram is a bicyclic antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI). It does not affect reuptake of norepinephrine or dopamine and has a relative lack of affinity for muscarinic, histamine, α_1- and α_2-adrenergic, and serotonin receptors.

Drug Characteristics: Citalopram

Dose Adjustment Hepatic	*Max* dose 20 mg po daily in hepatic impairment	**Absorption**	F = 80%; no effect of food on absorption
Dose Adjustment Renal	Use with caution in severe renal impairment	**Distribution**	Vd = 12 L/kg; 80% protein bound
Dialyzable	Not dialyzed	**Metabolism**	Hepatic >90%; substrate of CYP2C19 and 3A4/5
Pregnancy Category	C	**Elimination**	Fecal elimination is 20%, renal elimination is 20% (12-13% unchanged), with a half-life of 33-37 h
Lactation	Avoid	**Pharmacogenetics**	CYP2C19 poor metabolizers, *max* dose 20 mg/d
Contraindications	Hypersensitivity, concomitant use of pimozide, MAOIs	**Black Box Warnings**	Suicidal ideation; not approved for use in children

Medication Safety Issues: Citalopram

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	CeleXA	No	No	CeleBREX, ZyPREXA	No

Drug Interactions: Citalopram

Typical Agents	Mechanism	Clinical Management
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Dextroamphetamine, triptans, linezolid, lithium, MAOIs	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination), do not use MAOIs
CYP2C19 and CYP3A4/5 inducers	Increased citalopram metabolism reduces citalopram effectiveness	Monitor and consider dose increases of citalopram
CYP2C19 and CYP3A4/5 inhibitors	Decreased citalopram metabolism increases risk of citalopram toxicity	Monitor and consider dose decreases of citalopram

Adverse Reactions: Citalopram

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, dizziness, headache, insomnia, nausea, sedation, xerostomia	Agitation, anxiety, diaphoresis, diarrhea, disorder of ejaculation, fatigue, impotence, reduced libido, tremor	Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsades de pointes, agranulocytosis

Efficacy Monitoring Parameters. Improvement in symptoms of depression, panic disorder, OCD.

Toxicity Monitoring Parameters. Worsening of mental health symptoms, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

Clinical Pearls. If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Medication guide required when dispensing.

CLARITHROMYCIN: Biaxin, Various

Class: Macrolide Antibiotic

Dosage Forms. **Oral Tablet:** 250 mg, 500 mg; **Oral Suspension:** 125 mg/5 mL; 250 mg/5 mL; **Oral Tablet, Extended Release:** 500 mg

Dava generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute infective exacerbation of COPD: 250-500 mg po bid × 7-14 d
2. Community-acquired pneumonia, skin infection, sinusitis, pharyngitis: Adults, 250 mg po bid × 7-14 d or extended-release tablets, 1000 mg po daily for 7 d; Children ≥6 mo of age, 15 mg/kg/d divided q12h × 10 d
3. Disseminated infection due to *M. avium*-intracellulare group, prophylaxis-HIV infection, primary prevention and treatment: 500 mg po bid
4. *H. pylori* GI tract infection: 500 mg, bid × 10-14 d in combination with various other antibiotics and PPIs

Off-Label Uses.

1. Bacterial endocarditis prophylaxis for high-risk patients; dental, respiratory, or infected skin/skin structure or musculoskeletal tissue procedures: Adults, 500 mg po 30-60 min prior to procedure; Children, 15 mg/kg po 30-60 min prior to procedure

MOA. Clarithromycin binds to the 50S ribosomal subunit of the 70S ribosome of susceptible organisms, thereby inhibiting bacterial RNA-dependent protein synthesis.

Drug Characteristics: Clarithromycin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50%, extended release should be taken with food, immediate release can be taken without regard to food
Dose Adjustment Renal	CrCl <30 mL/min, reduce dose by 50% or increase interval to q24h	**Distribution**	Gastric tissue, lung, ear f uid, prostate, sputum, soft tissue
Dialyzable	Unknown	**Metabolism**	Hepatic; substrate of CYP3A4/5 to active metabolites, inhibitor of CYP3A4/5, P-glycoprotein
Pregnancy Category	C	**Elimination**	Renal elimination is 20-40% with a half-life of 5-7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to any macrolide or ketolide antibiotic; concomitant cisapride, pimozide, astemizole, terfenadine, ergotamine, or dihydroergotamine	**Black Box Warnings**	None

Medication Safety Issues: Clarithromycin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	No	Do not crush XL formulation	No	Claritin	No

Drug Interactions: Clarithromycin

Typical Agents	Mechanism	Clinical Management
Drugs known to prolong the QT interval	Increased risk of cardiotoxicity via additive QT prolongation	Avoid concurrent use or consider monitoring ECG
CYP3A4/5, P-glycoprotein substrates	Inhibition of CYP3A4/5, P-glycoprotein by clarithromycin reduces substrate metabolism and increases substrate toxicity	Monitor for toxicity and consider dose reductions of substrates; do not use substrates if narrow therapeutic index or if known to prolong QT interval
CYP3A4/5 inducers	Increased clarithromycin metabolism reduces clarithromycin effectiveness	Monitor and consider dose increases of clarithromycin
CYP3A4/5 inhibitors	Decreased clarithromycin metabolism increases risk of clarithromycin toxicity	Monitor and consider dose decreases of clarithromycin
Digoxin	Increased bioavailability and digoxin toxicity	Caution with concurrent use
Sulfonylureas	Increased risk of hypoglycemia	Use with caution and increase blood glucose monitoring
SSRIs	Increased risk of serotonin syndrome	Consider dose reduction of SSRI
Warfarin	Increased risk of bleeding via inhibition of warfarin metabolism	Monitor INR closely

Adverse Reactions: Clarithromycin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Taste disturbance	Headache, diarrhea, nausea, vomiting, rash	QT prolongation, Stevens-Johnson syndrome, anemia, neutropenia, thrombocytopenia, severe hypersensitivity, myasthenic crisis, elevated LFTs, hallucinations, nephrotoxicity

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Seek medical attention if heart palpitations, blistering skin rash, unusual bruising or bleeding, yellowing of skin or eyes, or extreme fatigue.

Key Patient Counseling Points. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with healthcare practitioner.

Clinical Pearls. Use with caution in severe renal, hepatic, or cardiac disease. Extended-release and immediate-release formulations are not interchangeable. Multiple drug interactions. *Max* dose in children, 1 g/d.

CLINDAMYCIN ORAL: Cleocin, Various

Class: Lincosamide Antibiotic

Dosage Forms. **Oral Capsule:** 75 mg, 150 mg, 300 mg; **Granules for Oral Solution:** 75 mg/5 mL

Greenstone generic 300 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bacterial infectious disease, susceptible infections due to anaerobic organisms, staphylococci, streptococci, pneumococci: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
2. Infection of skin and/or subcutaneous tissue: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
3. Infectious disease of abdomen: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
4. Lower respiratory tract infection: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
5. Pelvic inflammatory disease: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
6. Septicemia: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h

Off-Label Uses.

1. Bacterial vaginosis, oral treatment, pregnant women with symptomatic disease: 300 mg po bid × 7 d
2. Streptococcal pharyngitis, penicillin-allergic patients: Children, 20 mg/kg/d po in 3 divided doses (*max* 1.8 g/d)

MOA. Clindamycin is a semisynthetic 7-chloro-7-deoxylincomycin derivative that is active against most gram-positive organisms except enterococci and *C. difficile*. Gram-negative aerobes are resistant, but most anaerobes are sensitive. It inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit; it is bactericidal or bacteriostatic depending on the concentration, organism, and inoculums.

Drug Characteristics: Clindamycin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%, no food effect
Dose Adjustment Renal	If CrCl <30 mL/min, reduce dose by 50% or double interval	**Distribution**	Appendix, bone, gastric tissue, head and neck, sputum, peritoneal f uid, uterus
Dialyzable	Unknown	**Metabolism**	Minor hepatic
Pregnancy Category	B	**Elimination**	Renal elimination 5-28% with a half-life of 1.5-5 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to clindamycin	**Black Box Warnings**	Colitis

Medication Safety Issues: Clindamycin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Pediatric	No	Do not open capsules	No	Bleomycin, Clinoril, Claritin, clarithromycin	No

Drug Interactions: Clindamycin

Typical Agents	Mechanism	Clinical Management
Atracurium and nondepolarizing muscle relaxants	Clindamycin may have added effect on muscle contractility	Monitor for excessive neuromuscular blockade, consider dose reduction of muscle relaxant
Cyclosporine	Decreased bioavailability of cyclosporine; mechanism unknown	Monitor cyclosporine levels and consider dose adjustments
Erythromycin	Competition for the same binding site decreased antibiotic effect; theoretical additive effects on QT prolongation	Avoid concurrent use

Adverse Reactions: Clindamycin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, nausea, vomiting, rash	QT prolongation, Stevens-Johnson syndrome, pseudomembranous colitis, esophagitis

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Seek medical attention if heart palpitations, blistering skin rash, or profuse watery diarrhea.

Key Patient Counseling Points. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with healthcare practitioner. Take with full glass of water. Remain upright for 30 min after dose to minimize risk of GI ulceration.

Clinical Pearls. May resume normal activities after 24 h of antibiotics and if afebrile. Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*–associated diarrhea, which has been observed >2 m postantibiotic treatment. Also available as injectable, topical, and vaginal formulations. Common antibiotic for anaerobes infections above the diaphragm. Potential alternative in patients with gram-positive infection and allergy to penicillin (immediate-type hypersensitivity reactions).

CLINDAMYCIN TOPICAL: Cleocin T, Various

Class: Lincosamide Antibiotic

Dosage Forms. **Topical Foam:** 1%; **Topical Solution:** 1%; **Topical Gel:** 1%; **Topical Pad:** 1%; **Topical Lotion:** 1%

Common FDA Label Indication, Dosing, and Titration.

1. Acne vulgaris: Topical solution, lotion, gel; apply thin-film bid to affected areas; Foam: apply once daily to affected areas

Off-Label Uses.

1. Acneiform eruptions induced by epidermal growth factor receptor inhibitors: Topical gel or lotion; apply thin-film bid to affected areas

MOA. Clindamycin is a semisynthetic 7-chloro-7-deoxylincomycin derivative that is active against most gram-positive organisms except enterococci and *C. difficile*. Gram-negative aerobes are resistant, but most anaerobes are sensitive. It inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit; it is bactericidal or bacteriostatic depending on the concentration, organism, and inoculums.

1% Solution

1% Gel

Fougera generic pictured

Drug Characteristics: Clindamycin

Dose Adjustment Hepatic	Not required	**Absorption**	Not systemically absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not systemically absorbed
Dialyzable	Not systemically absorbed	**Metabolism**	Not systemically absorbed
Pregnancy Category	B	**Elimination**	Not systemically absorbed
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Clindamycin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
T	No	No	No	Bleomycin, Clinoril, Claritin, clarithromycin	No

Drug Interactions: Clindamycin. None known

Adverse Reactions: Clindamycin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dry skin	Itching pruritus, rash	

Efficacy Monitoring Parameters. Resolution of acne lesions.

Toxicity Monitoring Parameters. Seek medical attention if blistering skin rash.

Key Patient Counseling Points. Wash and dry face prior to application. Use on skin only, avoid eyes and mucous membranes, avoid cut or broken skin. Shake well before use. Liquid is flammable; avoid smoking while applying or exposure to heat or open flame. For the foam, apply to tissue and use that to apply to face.

Clinical Pearls. May have increased sensitivity to sun; may use sunscreen but wait 1-2 h after applying clindamycin topical solution. Also available as injectable, oral, and vaginal formulations.

CLOBAZAM: Onfi

Class: Anticonvulsant. C-IV

Dosage Forms. Oral Tablet: 5 mg, 10 mg, 20 mg; **Oral Suspension:** 2.5 mg/mL

Lundbeck 5 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Lennox-Gastaut syndrome: Children ≥2 y of age and ≤30 kg, 5 mg po daily, may titrate to 20 mg po daily; Adults and Children ≥2 y of age and >30 kg, 10 mg po daily, may titrate to 40 mg po daily

Off-Label Uses.

1. Alcohol withdrawal syndrome: 0.3-0.9 mg/kg/d po × 1 wk
2. Anxiety: 20-80 mg po daily (single or divided doses) × 5-14 d

MOA. Clobazam is a benzodiazepine. The exact mechanism of action for clobazam is not known, but is thought to involve potentiation of neurotransmission resulting from binding at the benzodiazepine site of the $GABA_A$ receptor.

Drug Characteristics: Clobazam

Dose Adjustment Hepatic	Initial dose no higher than 5 mg po daily; titrate slowly to *max* of 40 mg po daily	**Absorption**	F = 87%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 100 L; 90% protein bound
Dialyzable	Hemodialysis has no effect on plasma concentration of parent or metabolite	**Metabolism**	Extensive hepatic; substrate of CYP2C19, P-glycoprotein to active metabolite (norclobazam); inhibits CYP2D6, UGT1A4, UGT1A6, UGT2B4
Pregnancy Category	C	**Elimination**	Renal elimination is 82% with a half-life of 36-42 h for parent, 71-82 h for metabolite
Lactation	Compatible (small amounts expressed in breast milk)	**Pharmacogenetics**	Use with caution and reduce dose in CYP2C19 poor metabolizers
Contraindications	Hypersensitivity to clobazam	**Black Box Warnings**	None

Medication Safety Issues: Clobazam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	cloBAZam	No	No	clonazePAM	No

Drug Interactions: Clobazam

Typical Agents	Mechanism	Clinical Management
CYP2C19, P-glycoprotein inducers	Increased clobazam metabolism reduces clobazam effectiveness	Monitor and consider dose increases of clobazam
CYP2C19, P-glycoprotein inhibitors	Decreased clobazam metabolism increases risk of clobazam toxicity	Monitor and consider dose decreases of clobazam
CYP2D6, UGT1A4, UGT1A6, UGT2B4 substrates	Decreased substrate metabolism may result in substrate toxicity	Monitor and consider decreasing dose of substrate
Alcohol, opioids, and other CNS depressants	Additive CNS and respiratory depression	Avoid if possible and consider dose reductions of both agents
Phenytoin, fosphenytoin	Decreased metabolism of phenytoin	Monitor for phenytoin toxicity, reduce dose if necessary

Adverse Reactions: Clobazam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, drooling, ataxia, lethargy, respiratory infections, somnolence, fever	Dysarthria, insomnia, sedation, aggressive behavior, couth	Depression, Stevens-Johnson syndrome, suicidal attempts, toxic epidermal necrolysis

Efficacy Monitoring Parameters. Decrease in the frequency of seizures. Reduction in anxiety.

Toxicity Monitoring Parameters. Signs and symptoms of CNS depression, suicidal thoughts or behaviors, unusual changes in mood or behavior. Seek medical attention immediately if rash occurs, as significant risk of Stevens-Johnson syndrome.

Key Patient Counseling Points. Often causes lethargy and somnolence. Avoid alcohol while using. Avoid activities requiring mental alertness.

Clinical Pearls. Not indicated for children <2 y of age. Many drug-drug interactions; monitor concurrent drug use carefully. Medication guide required when dispensing.

CLOBETASOL: Temovate, Various

Class: Topical Corticosteroid

Dosage Forms. Cream: 0.05%; **Ointment:** 0.05%; **Topical Solution:** 0.05%; **Aerosol Foam:** 0.05%; **Gel:** 0.05%; **Shampoo:** 0.05%

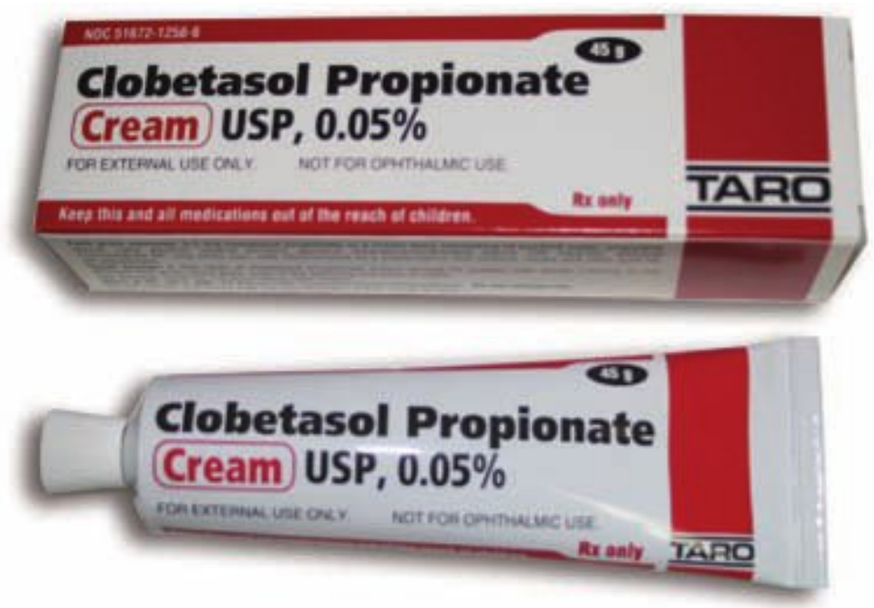
Common FDA Label Indication, Dosing, and Titration.

1. Skin disorders, corticosteroid responsive: Children ≥12 y of age and Adults, apply thin layer topically to affected area bid for a *max* of 2 wk
2. Plaque psoriasis: Children >12 y of age and adults, apply thin layer topically to affected area bid for a *max* of 2-4 wk

Off-Label Uses.

1. Oral lichen planus: Apply thin layer topically bid with antimycotics

MOA. Clobetasol has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.



Taro generic 0.05% cream pictured

Drug Characteristics: Clobetasol

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption unless covering large surface area or covering areas lacking skin integrity
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Clobetasol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Clobetasol. None known

Adverse Reactions: Clobetasol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Burning sensation, stinging, pruritus at site of administration, headache	Hypothalamic axis (HPA) suppression has been reported when used with occlusive dressings, over larger surface areas

Efficacy Monitoring Parameters. Improvement in clinical signs of skin disorder.

Toxicity Monitoring Parameters. Seek medical attention if severe skin irritation or symptoms worsen after administration.

Key Patient Counseling Points. Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

Clinical Pearls. Various dosage forms (foams, gels, shampoos, etc) available. Very high-potency corticosteroid. Application to large surface areas, prolonged use, and occlusive dressings may increase risk of systemic absorption and toxicity. Pediatric patients are more susceptible to systemic absorption.

CLONAZEPAM: Klonopin, Various

Teva generic pictured

Class: Benzodiazepine. C-IV

Dosage Forms. **Oral Tablet:** 0.5 mg, 1 mg, 2 mg; **Oral Tablet, Disintegrating:** 0.125 mg, 0.25 mg, 0.5 mg, 1 mg, 2 mg

Common FDA Label Indication, Dosing, and Titration.

1. Panic disorder: 0.25 mg po bid, may titrate by 0.125-0.25 mg po bid every 3 d to a *max* total daily dose of 1-4 mg (divided into 2-3 daily doses)
2. Seizure: Children ≥10 y of age or ≥30 kg and Adults, 0.5 mg po tid, may titrate by 0.125-0.25 mg po bid every 3 d to a *max* of 1-4 mg/d (divided into 2-3 daily doses); Children <10 y of age or <30 kg, 0.01-0.03 mg/kg/d po divided into 2-3 daily doses, may titrate by 0.25-0.5 mg po every 3 d to *max* of 0.1-0.2 mg/kg/d (divided into 3 daily doses)

Off-Label Uses.

1. Restless legs syndrome: 0.5-2 mg po qhs

MOA. Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

Drug Characteristics: Clonazepam

Dose Adjustment Hepatic	Decrease usual dose by 50%	**Absorption**	F = 90%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.5-3 L; 85% protein bound
Dialyzable	Supplemental dose not required	**Metabolism**	Hepatic; substrate of CYP3A4/5
Pregnancy Category	D	**Elimination**	Renal elimination is 1% with a half-life of 30-40 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to benzodiazepines, narrow-angle glaucoma, liver disease	**Black Box Warnings**	None

Medication Safety Issues: Clonazepam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	ClonazePAM	Oral disintegrating tablets	No	cloBAZam, cloNIDine, clorazepate, cloZAPine, LORazepam	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium.

Drug Interactions: Clonazepam

Typical Agents	Mechanism	Clinical Management
Alfentanil, opioids, and other respiratory depressants	Additive respiratory depression	Avoid if possible and consider dose reductions of both agents
CYP3A4/5 inducers	Increased clonazepam metabolism reduces clonazepam effectiveness	Monitor and consider dose increases of clonazepam
CYP3A4/5 inhibitors	Decreased clonazepam metabolism increases risk of clonazepam toxicity	Monitor and consider dose decreases of clonazepam
Theophylline	Decreased clonazepam effectiveness via inhibition of adenosine receptors	Monitor and consider dose increases for clonazepam

Adverse Reactions: Clonazepam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Ataxia, lethargy, somnolence, weight gain	Tachycardia, palpitations, nausea and vomiting, blurred vision	Seizures, mania, depression, withdrawal symptoms

Efficacy Monitoring Parameters. Reduction in anxiety symptoms or seizures.

Toxicity Monitoring Parameters. Seek medical attention if severe drowsiness, slow or rapid heartbeat or skipped beats, thoughts of suicide.

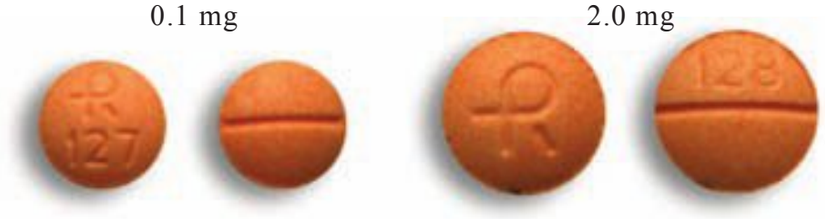
Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Allow orally disintegrating tablet to dissolve on your tongue. Avoid alcohol.

Clinical Pearls. Consider dose reductions of benzodiazepine in hepatic impairment. Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. Medication guide required when dispensing. Higher abuse potential among benzodiazepines.

CLONIDINE: Catapres, Various

Class: α_2-Adrenergic Agonist

Dosage Forms. **Oral Tablet:** 0.1 mg, 0.2 mg, 0.3 mg; **Oral Tablet, Extended Release:** 0.1 mg, 0.2 mg; **Transdermal Patch:** 0.1 mg/24 h, 0.2 mg/24 h, 0.3 mg/24 h



Actavis generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Attention-deficit hyperactivity disorder: Children >6 y of age, 0.1 mg extended-release tablet po qhs, may titrate in increments of 0.1 mg/d at weekly intervals to desired effect; give doses >0.1 mg/d in 2 divided doses; *max* dose 0.4 mg/d
2. Essential hypertension: 0.1 mg/d transdermal patch applied every 7 d, may titrate by 0.1 mg/d transdermal patch increments every 1-2 wk; *max* 0.6 mg/d every 7 d
3. Hypertension: 0.1 mg po bid, may titrate by 0.1 mg/d at weekly intervals, to 0.2-0.6 mg in 2 divided doses, *max* 2.4 mg/d

Off-Label Uses.

1. Hot sweats: 0.1 mg/d transdermal patch every 7 d or 0.2 mg po daily
2. Nicotine dependence: 0.1-0.2 mg/24 h transdermal patch daily or 0.1-0.45 mg po daily
3. Spasticity: 0.05-0.4 mg po daily in divided doses

MOA. Clonidine stimulates postsynaptic α_2-adrenergic receptors in the CNS by activating inhibitory neurons to decrease sympathetic outflow. Clonidine is not a complete agonist, so some of its effects might result from antagonist actions at presynaptic α-receptors. These actions reduce peripheral vascular resistance, renal vascular resistance, HR, and BP.

Drug Characteristics: Clonidine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 75-100% immediate-release tablet, F = 60% patch; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.9 L/kg; 20-40% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism, unknown pathway
Pregnancy Category	C	**Elimination**	Renal elimination of clonidine is 40-60% with a half-life of 12.5-16 h (41 h in patients with renal disease)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	Epidural use

Medication Safety Issues: Clonidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
TTS	CloNIDine	Extended-release tablets	No	Clomid, clomiPHENE, clonazePAM, cloZAPine, KlonoPIN, quiNIDine	Avoid clonidine as a first-line antihypertensive. High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension.

Drug Interactions: Clonidine

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of clonidine	Avoid concurrent use or monitor BP
TCAs	Decreased antihypertensive effect of clonidine by increasing release of norepinephrine	Avoid concurrent use or monitor BP
Beta-blockers, calcium channel blockers	Increased risk of hypotension and sinus bradycardia	Avoid concurrent use or monitor BP and HR
Cyclosporine	Increased risk of cyclosporine toxicity	Monitor serum cyclosporine levels

Adverse Reactions: Clonidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Feeling nervous, headache, somnolence, erythema (patch), xerostomia	Bradycardia, constipation, contact dermatitis (patch), fatigue, hypotension, increased body temperature, irritability, nausea, palpitations, rash, rebound hypertension, sedation, tachycardia, urticaria	AV block

Efficacy Monitoring Parameters. Decreased BP or improvement of mental and behavioral symptoms of ADHD.

Toxicity Monitoring Parameters. Rebound hypertension, increased HR, palpitations, syncope.

Key Patient Counseling Points. Avoid alcohol, CNS depressants. Caution with driving and other tasks requiring alertness. Swallow extended-release tablet whole, may be taken with or without food. Apply patch to hairless area of intact skin on upper outer arm or chest; rotate patch location. If patch loosens during the 7-d wearing, secure adhesive cover. Report signs/symptoms of hypotension, exacerbation of angina peripheral edema, fatigue, hypotension, or hepatic dysfunction with initial dosing and dose changes. Avoid abrupt discontinuation to avoid rebound hypertension.

Clinical Pearls. Safety and efficacy of the immediate-release tablet for the treatment of hypertension not established in children. Extended-release tablets and immediate-release tablet formulation are not interchangeable. Injectable formulation available for epidural infusion (pain management).

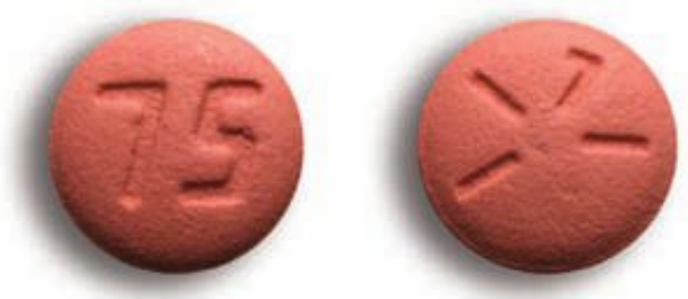
CLOPIDOGREL: Plavix, Various

Class: Platelet Aggregation Inhibitor

Dosage Forms. **Oral Tablet:** 75 mg, 300 mg

Common FDA Label Indication, Dosing, and Titration.

1. Acute ST and non–ST segment elevation myocardial infarction: 300-600 mg po loading dose, followed by 75 mg po daily (in combination with aspirin for those not at risk of bleeding)
2. Thrombosis prevention in arteriosclerotic vascular disease, following stroke, in peripheral arterial occlusive disease: 75 mg po daily



Bristol-Myers Squibb/Sanofi Aventis
75 mg pictured

Off-Label Uses.

1. Thrombosis prevention in atrial fibrillation or following percutaneous coronary intervention: 75 mg po daily (in combination with aspirin for those not at risk of bleeding)

MOA. Clopidogrel is an antiplatelet agent that prevents platelet aggregation by direct inhibition of ADP binding to receptor sites, inhibiting subsequent activation of the glycoprotein IIb/IIIa complex. This action is irreversible; therefore, platelets exposed to clopidogrel are inhibited for their life spans.

Drug Characteristics: Clopidogrel

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Prodrug, requires activation by CYP2C19; substrate of CYP2C19, inhibitor of CYP2B6, CYP2C8
Pregnancy Category	B	**Elimination**	Renal elimination of clopidogrel is 50% with a half-life of 6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2C19 poor metabolizers; increased risk of cardiovascular events due to reduced efficacy of clopidogrel; consider alternative treatment or a higher dose
Contraindications	Hypersensitivity to clopidogrel and active bleeding	**Black Box Warnings**	Reduced CYP2C19 function

Medication Safety Issues: Clopidogrel

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Elavil, Paxil, Pradaxa	No

Drug Interactions: Clopidogrel

Typical Agents	Mechanism	Clinical Management
Amiodarone, azole antifungals, calcium channel blockers, cimetidine, fluoxetine, fluvoxamine, PPIs	Decreased platelet inhibitory effect of clopidogrel	Avoid concurrent use or monitor for signs/symptoms of thrombus formation
Aspirin, cilostazol, direct thrombin inhibitors, fibrinolytics, fondaparinux, low-molecular-weight heparin, NSAIDs, SSRIs, ticlopidine, unfractionated heparin, warfarin	Increased risk of bleeding	Monitor for signs/symptoms of bleeding
CYP2B6, CYP2C8 substrates	Reduced metabolism of substrates via inhibition of CYP2B6, CYP2C8	Monitor and consider substrate dose reductions
CYP2C19 inducers	Increased clopidogrel activation increases clopidogrel toxicity	Monitor and consider decreasing dose of clopidogrel
CYP2C19 inhibitors	Decreased clopidogrel activation decreases clopidogrel efficacy	Monitor and consider increasing dose of clopidogrel

Adverse Reactions: Clopidogrel

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Arthralgia, backache, epistaxis, gastritis, headache, hypertension, pruritus	Agranulocytosis, Stevens-Johnson syndrome, GI hemorrhage, GI ulcer, pancytopenia, thrombotic thrombocytopenic purpura

Efficacy Monitoring Parameters. Prevention of thrombotic events.

Toxicity Monitoring Parameters. Signs/symptoms of bleeding, especially with concomitant anticoagulant therapy.

Key Patient Counseling Points. Report signs/symptoms of bleeding, especially if used concomitantly with anticoagulant therapy. Do not stop therapy abruptly without first talking with prescriber to minimize the risk of re-thrombosis, particularly after stent placement. Clopidogrel should be discontinued 5 d prior to elective surgery, if an antiplatelet effect is not desired.

Clinical Pearls. Safety and efficacy not established in pediatric patients. Clopidogrel effectiveness is dependent on its activation to an active metabolite by CYP2C19. In patients who are CYP2C19 poor metabolizers or taking concurrent CYP2C19 inhibitors, clopidogrel at recommended doses forms less of the active metabolite and has a smaller effect on platelet function. Compared with normal metabolizers, poor CYP2C19 metabolizers with acute coronary syndrome, or undergoing percutaneous coronary intervention treated with clopidogrel at recommended doses, exhibit higher cardiovascular event rates. Consider alternative treatment or a higher dose in CYP2C19 poor metabolizers.

CLOTRIMAZOLE/BETAMETHASONE: Lotrisone, Various

Class: Anti-infective/Anti-inflammatory Combination

Dosage Forms. **Topical Cream:** (Clotrimazole/Betamethasone) 1%/0.05%**, Topical Lotion:** (Clotrimazole/Betamethasone) 1%/0.05%

Common FDA Label Indication, Dosing, and Titration.

1. Tinea: Adults and children >12 y, apply to affected area bid, for a *max* of 2 wk (for tinea corporis or tinea cruris) or 4 wk (for tinea pedis)

Off-Label Uses. None

MOA. Clotrimazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability. Betamethasone dipropionate is a corticosteroid that stimulates synthesis of enzymes thought to be responsible for anti-inflammatory effects.

Taro generic 1%/0.05% cream pictured

Drug Characteristics: Betamethasone/Clotrimazole

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption
Dose Adjustment Renal	Not required	**Distribution**	Minimal absorption
Dialyzable	Unknown	**Metabolism**	Minimal absorption
Pregnancy Category	C	**Elimination**	Minimal absorption
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to clotrimazole or betamethasone	**Black Box Warnings**	None

Medication Safety Issues: Betamethasone/Clotrimazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Co-trimoxazole	No

Drug Interactions: Betamethasone/Clotrimazole. None known

Adverse Reactions: Betamethasone/Clotrimazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dry skin	Rash, HPA suppression has been reported in children, therefore not recommended in children <12 y of age

Efficacy Monitoring Parameters. Resolution of erythema and pruritus. Improvement in erythema and pruritus usually occurs within 3-5 d. If no improvement is seen after 1 wk of treatment for tinea cruris or tinea corporis, or after 2 wk of treatment for tinea pedis, then the diagnosis should be reviewed.

Toxicity Monitoring Parameters. Seek medical attention if severe skin irritation or rash. Various cortisol tests could be utilized to evaluate HPA suppression.

Key Patient Counseling Points. Apply thin layer to affected area. If using lotion, shake well before use.

Clinical Pearls. Patients receiving the combination therapy show an earlier, better clinical response than patients treated with clotrimazole cream or betamethasone cream alone. Cure rates with clotrimazole/betamethasone are at least as good or better as compared to clotrimazole alone. Do not use with occlusive dressings or on larger areas. This can lead to systemic absorption of betamethasone and HPA suppression.

CODEINE: Tylenol with Codeine, Various

Class: Opioid. C-II (when in combination with acetaminophen, C-III)

Dosage Forms. Oral Tablet (Codeine Alone): 15 mg, 30 mg, 60 mg; **Oral Solution (Codeine Alone):** 30 mg/5 mL; **Oral Tablet (With Acetaminophen):** Acetaminophen/Codeine 300 mg/15 mg, Acetaminophen/Codeine 300 mg/30 mg, Acetaminophen/Codeine 300 mg/60 mg; **Oral Elixir, Oral Solution (With Acetaminophen):** Acetaminophen/Codeine 120 mg/12 mg per 5 mL

300 mg/30 mg

Teva generic pictured

C

Common FDA Label Indication, Dosing, and Titration.

1. Pain: Adults, 15-60 mg po q4h prn; with acetaminophen 300-1000 mg (*max* 4000 mg/d); Children 3-6 y of age, 12 mg po 3-4 times a day prn, with acetaminophen 120 mg/dose; Children 7-10 y of age, 24 mg po 3-4 times a day prn, with acetaminophen 240 mg/dose

Off-Label Uses. None

MOA. Codeine is 3-methoxymorphine, a phenanthrene opioid with very low affinity for opioid receptors. Its analgesic activity appears to result from conversion to morphine.

Drug Characteristics: Codeine

Dose Adjustment Hepatic	Avoid chronic use in hepatic impairment	**Absorption**	Well absorbed; food has no effect on absorption
Dose Adjustment Renal	Codeine: CrCl 10-50 mL/min, 75% of dose; CrCl <10 mL/min, 50% of dose	**Distribution**	Vd = 2.6 L/kg; 7-25% protein bound
Dialyzable	Unknown	**Metabolism**	Codeine is a prodrug that requires activation by CYP2D6 to morphine; substrate of CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination approaches 100% with a half-life of 2-4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 variants with altered response
Contraindications	Hypersensitivity to codeine	**Black Box Warnings**	Hepatotoxicity

Medication Safety Issues: Codeine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Tylenol 3 and Tylenol	No	No	Yes (opioids)	Cardene, Lodine	No

Drug Interactions: Codeine

Typical Agents	Mechanism	Clinical Management
Alcohol, opioids, and other CNS depressants	Additive CNS and respiratory depression	Avoid if possible and consider dose reductions of both agents
Buprenorphine, opioid agonists/ antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP2D6 inhibitors	Decreased effectiveness of codeine; prevents conversion of codeine to active metabolite, morphine	Monitor and consider increasing dose of codeine or choose alternative analgesic agent

Adverse Reactions: Codeine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, vomiting, constipation, somnolence	Pruritus, euphoria, dizziness	Stevens-Johnson syndrome, GI bleeding, elevated liver functions, thrombocytopenia, physical dependence, tolerance, respiratory depression

Efficacy Monitoring Parameters. Decreased pain.

Toxicity Monitoring Parameters. LFTs, SCr, if chronic use; severe skin rash, black tarry stools, excessive drowsiness, yellowing of eyes of skin, change in urination.

Key Patient Counseling Points. If using chronically, use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

Clinical Pearls. Use caution in elderly, appear more sensitive to the effects. Use of CNS depressants with caution, may have additive effects. Tolerance and physical dependence may occur, avoid abrupt discontinuation. Oral solution contains 7% alcohol. Patients with multiple CYP2D6 gene copies metabolize codeine more rapidly (ultrarapid metabolism), whereas patients who lack functional CYP2D6 genes do not metabolize codeine to morphine and do not experience analgesic effects. Multiple CYP2D6 gene copies occur in 4-5% of Caucasians and is absent in 5-10% of the Caucasian population. In ultrarapid metabolizers, pediatric deaths post-tonsillectomy have been reported. CYP2D6 inhibitors, especially SSRIs, may also prevent activation of codeine to morphine. Codeine also available in combination with guaifenesin for cough.

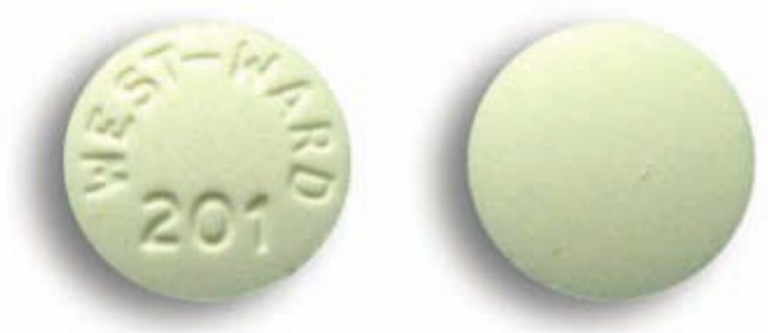
COLCHICINE: Colcyrs, Various

Class: Antigout

Dosage Forms. **Oral Tablet:** 0.6 mg

Common FDA Label Indication, Dosing, and Titration.

1. Gout, acute: 1.2 mg po at the first sign of a flare followed by 0.6 mg 1 h later; *max* 1.8 mg over 1 h
2. Gout, prophylaxis: 0.6 mg po daily to bid, *max* of 1.2 mg/d or onset of diarrhea
3. Familial Mediterranean fever: Children 4-6 y of age, 0.3-1.8 mg po daily; Children 6-12 y, 0.9-1.8 mg po daily; Children ≥12 y of age and Adults, 1.2-2.4 mg po daily, increase or decrease dose in increments of 0.3 mg/d



West-ward generic 0.6 mg pictured

Off-Label Uses.

1. Amyloidosis: 0.6 mg po bid
2. Constipation: 0.6 mg po q30 min until onset of diarrhea

MOA. Exact mechanism unknown. In patients with gout, may interrupt the cycle of monosodium urate crystal deposition in joint tissues and the resultant inflammatory response that initiates and sustains an acute attack. Colchicine also inhibits urate crystal deposition, which is enhanced by a low pH in the tissues, probably by inhibiting oxidation of glucose and subsequent lactic acid production in leukocytes.

Drug Characteristics: Colchicine

Dose Adjustment Hepatic	Severe hepatic failure, do not repeat gout f are courses more than once every 2 wk	**Absorption**	F = 45%, no effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, for gout f are, do not repeat course more than once every 2 wk	**Distribution**	Vd = 5-8 L/kg, 39% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Partial hepatic; substrate of CYP3A4/5, P-glycoprotein
Pregnancy Category	C	**Elimination**	Renal elimination is 40-65% with a half-life of 26-32 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to colchicine; concurrent use with strong CYP3A4/5 inhibitors in patients with renal or hepatic failure	**Black Box Warnings**	None

Medication Safety Issues: Colchicine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Cortrosyn	No

Drug Interactions: Colchicine

Typical Agents	Mechanism	sClinical Management
CYP3A4/5, P-glycoprotein inducers	Increased colchicine metabolism reduces colchicine effectiveness	Monitor and consider dose increases of colchicine
CYP3A4/5, P-glycoprotein inhibitors	Decreased colchicine metabolism increases risk of colchicine toxicity	Monitor and consider dose decreases of colchicine, particularly if renal or hepatic dysfunction exists
Lipid-lowering agents (fibrates, statins)	Coadministration of colchicine and lipid-lowering agents may result in myopathy and rhabdomyolysis; mechanism unknown	Avoid concurrent use

Adverse Reactions: Colchicine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea	Vomiting	Agranulocytosis, rhabdomyolysiss

Efficacy Monitoring Parameters. Resolution of clinical signs and symptoms of gout (pain, stiffness, swelling).

Toxicity Monitoring Parameters. CBC, alkaline phosphatase at baseline and periodically during treatment. Instruct patients to discontinue the medication immediately and seek medical attention if signs and symptoms of agranulocytosis (severe neutropenia), or myotoxicity (including rhabdomyolysis). Monitor renal and hepatic function.

Key Patient Counseling Points. Instruct patient on appropriate dosing strategy for gout flares (dosing to symptom relief or onset of adverse effects, particularly diarrhea).

Clinical Pearls. Colchicine is a natural alkaloid found in plants such as the autumn crocus (*Colchicum autumnale*) and glory lily (*Gloriosa superba*). Medication guide required with dispensing.

COLESEVELAM: Welchol

Class: Hypolipidemic, Bile Acid Sequestrant

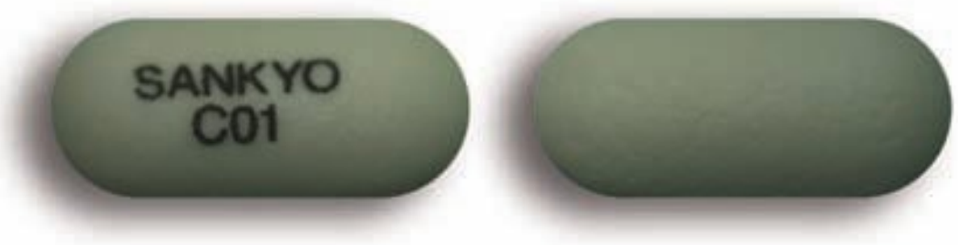
Dosage Forms. **Oral Tablet:** 625 mg; **Granules for Oral Suspension:** 3.75 g/packet

Common FDA Label Indication, Dosing, and Titration.

1. Primary hyperlipidemia: 1875 mg (3 tablets or 1.875 g powder packet) po bid or 3750 mg (6 tablets or 3.75 g powder packet) po daily

Off-Label Uses.

1. Familial hypercholesterolemia: 1875 mg (3 tablets or 1.875 g powder packet) po bid or 3750 mg (6 tablets or 3.75 g powder packet) po daily



Daichi-Sankyo 625 mg pictured

C

MOA. Colesevelam is a nonabsorbed, polymeric, lipid-lowering agent that binds intestinal bile acids, resulting in the increased clearance of LDL-cholesterol and a reduction in total cholesterol. Unlike cholestyramine and colestipol, colesevelam is not an anion exchange resin but binds bile acids and impedes their reabsorption.

Drug Characteristics: Colesevelam

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	B	**Elimination**	Fecal elimination is >99% and renal elimination is 0.05%
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	History of bowel obstruction, hypertriglyceridemia-induced pancreatitis; serum triglyceride level >500 mg/dL	**Black Box Warnings**	None

Medication Safety Issues: Colesevelam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Tablets (use granules instead)	No	No	No

Drug Interactions: Colesevelam

Typical Agents	Mechanism	Clinical Management
Antidiabetic drugs, diltiazem, ezetimibe, fibrates, levothyroxine, mycophenolate, oral contraceptives	Decreased bioavailability of colesevelam due to binding and decreased absorption	Take drug 4 h prior to colesevelam
Cyclosporine, phenytoin	Decreased bioavailability of cyclosporine and phenytoin due to binding and decreased absorption	Take drug 4 h prior to colesevelam; monitor drug serum levels
Warfarin	Decreased bioavailability of warfarin due to binding and decreased absorption	Take warfarin 4 h prior to colesevelam; monitor INR values

Adverse Reactions: Colesevelam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation	Asthenia, nasopharyngitis, myalgia, nausea, hypertension, hypertriglyceridemia, hypoglycemia	Pancreatitis, bowel obstruction

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

Toxicity Monitoring Parameters. Signs/symptoms of GI side effects, vitamin A, D, E, or K deficiencies.

Key Patient Counseling Points. Should be used together with diet and exercise to lower cholesterol levels. Empty contents of powder packet into a glass and mix with 120-240 mL of water; stir well and drink. Oral suspension should not be taken in its dry form. Take with a meal. Tablet should be swallowed with liquid (water, milk, or juice). May be dosed concomitantly with an HMG-CoA reductase inhibitor.

Clinical Pearls. Safety and efficacy not established in pediatric patients <10 y of age or in premenarcheal girls. Patients with difficulty swallowing should use oral suspension instead of tablets.

CONJUGATED ESTROGENS: Premarin

Class: Estrogen Hormone

Dosage Forms. Oral Tablet: 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg

Wyeth pictured

Common FDA Label Indication, Dosing, and Titration.

1. Abnormal vasomotor function (menopause), atrophy of vagina or vulva, postmenopausal osteoporosis prophylaxis, female hypogonadism syndrome: 0.3 mg po daily, continuously or cyclically; adjust dose to individual response
2. Primary ovarian failure: 1.25 mg po daily cyclically (3 wk on, 1 wk off); adjust dose to individual response

Off-Label Uses. None

MOA. Estrogens are largely responsible for the development and maintenance of the female reproductive system and secondary sexual characteristics. The primary source of estrogen in normally cycling adult women is the ovarian follicle. After menopause, most endogenous estrogen is produced by conversion of androstenedione to estrone by peripheral tissues. Estrogens act through binding to nuclear receptors in estrogen-responsive tissues. Circulating estrogens modulate the pituitary secretion of the gonadotropins, luteinizing hormone (LH), and follicle-stimulating hormone (FSH), through a negative-feedback mechanism. Estrogens act to reduce the elevated levels of these gonadotropins seen in postmenopausal women.

Drug Characteristics: Conjugated Estrogens

Dose Adjustment Hepatic	Avoid in severe liver dysfunction	**Absorption**	Well absorbed, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Largely distributed; bound to sex hormone proteins
Dialyzable	Not dialyzable	**Metabolism**	Hepatic; substrate of CYP3A4/5 and 1A2
Pregnancy Category	X	**Elimination**	Primary renal elimination with a half-life of 26 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, undiagnosed abnormal genital bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of deep vein thrombosis or pulmonary embolism, severe liver dysfunction, known or suspected pregnancy	**Black Box Warnings**	Breast cancer, cardiovascular disease, endometrial cancer, dementia risks

Medication Safety Issues: Conjugated Estrogens

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Primaxin, Provera, Remeron	Avoid oral and topical patch.

Drug Interactions: Conjugated Estrogens

Typical Agents	Mechanism	Clinical Management
CYP3A4/5, 1A2 inducers	Increased estrogen metabolism reduces estrogen effectiveness	Monitor and consider dose increases of estrogen
CYP3A4/5, 1A2 inhibitors	Decreased estrogen metabolism increases risk of estrogen toxicity	Monitor and consider dose decreases of estrogen
Levothyroxine	Estrogen increases serum thyroxine-binding globulin, reducing free thyroxine resulting in hypothyroid effects	Measure TSH and adjust dose if necessary

Adverse Reactions: Conjugated Estrogens

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight change, headache, migraine, depression, disorder of menstruation, breast pain	Edema, vasodilation, abdominal pain, hirsutism, diarrhea, nausea, stomach cramps, vomiting, backache	Heart disease, hypertension, myocardial infarction, breast cancer, diabetes mellitus, hypercalcemia, venous thromboembolism, anaphylaxis, cerebrovascular accident, cervical cancer, malignant neoplasm of endometrium of corpus uteri, ovarian cancer, pulmonary embolism

Efficacy Monitoring Parameters. Resolution of clinical signs of abnormal bleeding or hot flashes or other symptoms, prevention of osteoporosis.

Toxicity Monitoring Parameters. Monitor BMD; conduct diagnostic evaluation to rule out malignancy in the event of persistent or recurring vaginal bleeding.

Key Patient Counseling Points. Discuss potential long-term adverse effects of hormone therapy including myocardial infarction, stroke, deep vein thrombosis, pulmonary embolism, and breast cancer. Take at bedtime to minimize side effects. Take with or without meals.

Clinical Pearls. Injectable and vaginal cream is also available for other indications requiring estrogen replacement therapy. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk (over placebo) of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT has been shown in postmenopausal women. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman. In postmenopausal women with a uterus, a progestin (eg, medroxyprogesterone) should be added to estrogen to reduce the risk of endometrial cancer. Increased incidence of dementia was observed in women ≥65 y of age taking estrogens. Also available in combination with bazedoxifene (Duavee) for osteoporosis prevention and vasomotor symptoms.

CYANOCOBALAMIN: Cobolin-M, Various

Class: Essential B Vitamin (B_{12})

Dosage Forms. Injection Solution: 1000 mcg/mL; **Mucous Membrane Lozenge/Troche:** 50 mcg, 100 mcg, 250 mcg, 500 mcg; **Oral Tablet:** 50 mcg, 100 mcg, 250 mcg, 500 mcg, 1 mg; **Oral Tablet, Extended Release:** 1 mg; **Sublingual Tablet:** 2.5 mg; **Nasal Solution:** 500 mcg/0.1 mL

Common FDA Label Indication, Dosing, and Titration.

1. Cobalamin deficiency, normal absorption: Oral, 1000 mcg po daily; Nasal, 500 mcg in 1 nostril once weekly
2. Cobalamin deficiency, malabsorption: 100 mcg IM or deep subq injection daily for 6-7 d, then 100 mcg monthly for life

Off-Label Uses. None

MOA. B_{12} is required for the synthesis of the amino acid methionine from homocysteine. A deficiency of B_{12} results in hyperhomocysteinemia and a decrease in methionine. Since methionine is required for DNA synthesis, B_{12} deficiency also results in decreased DNA synthesis, which presents clinically as macrocytic anemia when red blood cells are unable to extrude their nucleus.

Drug Characteristics: Cyanocobalamin

Dose Adjustment Hepatic	Not required	**Absorption**	Oral: Absorption is poor and requires intrinsic factor, patients without intrinsic factor require IM supplementation; IM: approaches 100%
Dose Adjustment Renal	Not required	**Distribution**	Stored in the liver and most tissues
Dialyzable	Not dialyzable	**Metabolism**	Enterohepatic cycling occurs
Pregnancy Category	C	**Elimination**	Dose dependent, renal 50-98% with 100-1000 mcg IM dose
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cyanocobalamin or cobalt	**Black Box Warnings**	None

American Regent 1000 mcg/mL generic pictured

Medication Safety Issues: Cyanocobalamin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	ER product	No	No	No

Drug Interactions: Cyanocobalamin. None known

Adverse Reactions: Cyanocobalamin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site pain, arthralgia, fatigue, dizziness, headache	Edema	Anaphylaxis, worsening of heart failure, angioedema

Efficacy Monitoring Parameters. Baseline and periodic B_{12} and folic acid levels, intrinsic factor, normalization of MCV, normalization of Hgb, resolution of symptoms of anemia (fatigue, shortness of breath).

Toxicity Monitoring Parameters. Seek medical attention if severe shortness of breath, swelling, skin rash, or hives.

Key Patient Counseling Points. May require several weeks for maximum effect. Take extended-release products with food. Avoid alcohol as it inhibits the absorption of B_{12}.

Clinical Pearls. Drugs that interfere with folate metabolism (methotrexate, hydroxyurea, pemetrexed) will cause an elevated MCV in the absence of vitamin B deficiency. Patients on pemetrexed receive B_{12} to prevent toxicity. Metformin decreases B_{12} concentrations.

CYCLOBENZAPRINE: Flexeril, Various

Class: Centrally Acting Skeletal Muscle Relaxant

Dosage Forms. **Oral Tablet:** 5 mg, 7.5 mg, 10 mg; **Oral Capsule, Extended Release:** 15 mg, 30 mg

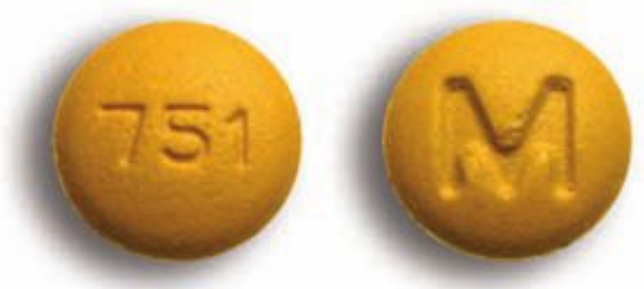
Common FDA Label Indication, Dosing, and Titration.

1. Skeletal muscle spasm: 5 mg po tid; may titrate to 10 mg po tid, may treat up to 2-3 wk

Off-Label Uses.

1. Temporomandibular joint disorder, 10 mg po daily × 3 wk

MOA. Cyclobenzaprine relieves skeletal muscle spasm of local origin without interfering with muscle function. It is ineffective in muscle spasm due to CNS disease. Evidence suggests that the net effect of cyclobenzaprine is a reduction in tonic somatic motor activity, influencing both gamma (γ) and alpha (α) motor systems.



Mylan generic 10 mg pictured

Drug Characteristics: Cyclobenzaprine

Dose Adjustment Hepatic	Mild hepatic dysfunction, 5 mg po daily; moderate, severe hepatic dysfunction, avoid	**Absorption**	F = 33-55%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP1A2
Pregnancy Category	B	**Elimination**	Renal elimination is 50% with a half-life of 18 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cyclobenzaprine, concomitant MAOI use, heart failure, acute coronary phase of AMI, heart block	**Black Box Warnings**	None

Medication Safety Issues: Cyclobenzaprine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Extended-release capsules	No	CycloSERINE, Floxin	Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures.

Drug Interactions: Cyclobenzaprine

Typical Agents	Mechanism	Clinical Management
CYP1A2 inducers	Increased cyclobenzaprine metabolism reduces cyclobenzaprine effectiveness	Monitor and consider dose increases of cyclobenzaprine
CYP1A2 inhibitors	Decreased cyclobenzaprine metabolism increases risk of cyclobenzaprine toxicity	Monitor and consider dose decreases of cyclobenzaprine
CNS depressants (opioids, benzodiazepines, alcohol)	Additive sedative effects	Avoid concurrent use or monitor carefully for signs of toxicity

Adverse Reactions: Cyclobenzaprine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Xerostomia, headache, drowsiness	Constipation, indigestion, nausea, pharyngeal dryness, asthenia, dizziness, confusion, blurred vision	Cardiac dysrhythmia, cholestasis, hepatitis, jaundice, anaphylaxis, immune hypersensitivity reaction

Efficacy Monitoring Parameters. Reduction in pain and muscle spasms.

Toxicity Monitoring Parameters. Seek medical attention if symptoms of hepatic failure occur during therapy with this agent.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Take extended-release capsule same time each day.

Clinical Pearls. Cyclobenzaprine is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2-3 wk). Should be used with caution in patients with glaucoma, increased IOP, urinary retention, etc, as cyclobenzaprine has anticholinergic-like effects. Avoid use in elderly, may be more sensitive to effects.

CYCLOSPORINE OPHTHALMIC: Restasis

Class: Calcineurin Inhibitor

Dosage Forms. Ophthalmic Emulsion: 0.5%

Common FDA Label Indication, Dosing, and Titration.

1. Keratoconjunctivitis sicca, when associated ocular inflammation results in scanty tear production: 1 drop in affected eye(s) q12h

Off-Label Uses. None

MOA. Ocular inflammation associated with keratoconjunctivitis sicca results in reduced tear production. Cyclosporin binds to cyclophilin, which inhibits the antigenic response of helper T lymphocytes which reduces the production of interleukin-2 and suppresses interferon-γ. Inhibition of the immune response limits inflammation.

Allergan 0.05% emulsion pictured

Drug Characteristics: Cyclosporine Ophthalmic

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption
Dose Adjustment Renal	Not required	**Distribution**	Minimal absorption
Dialyzable	Not dialyzable	**Metabolism**	Minimal absorption
Pregnancy Category	C	**Elimination**	Minimal absorption
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cyclosporine, active ocular infection	**Black Box Warnings**	None

Medication Safety Issues: Cyclosporine Ophthalmic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	CycloSPORINE	No	No	CycloSERINE	No

Drug Interactions: Cyclosporine Ophthalmic. None known

Adverse Reactions: Cyclosporine Ophthalmic

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Burning sensation in eye	Conjunctivitis, blurred vision	Hypersensitivity

Efficacy Monitoring Parameters. Improved tear production.

Toxicity Monitoring Parameters. Severe burning of the eye, active ocular infection.

Key Patient Counseling Points. This medicine comes in single-use packages. After you open a single-use package, use the medicine right away. Mix the medicine well just before using it. To do this, turn the single-use package upside down a few times. Remove contact lenses before using this medicine. Wait at least 15 min before inserting contact lenses after using the medicine. May be used with artificial tears as long as there is 15-min interval in between.

Clinical Pearls. Not for use in children <16 y of age. Oral formulation available for transplant rejection prevention.

DABIGATRAN: Pradaxa

Class: Anticoagulant

Dosage Forms. Oral Capsule: 75 mg, 150 mg

Common FDA Label Indication, Dosing, and Titration.

1. Treatment and prevention of initial or recurrent deep venous thrombosis and pulmonary embolism: 150 mg po bid (after 5-10 d treatment with parenteral anticoagulant)
2. Prevention of stroke and systemic embolism in patient with nonvalvular atrial fibrillation: 150 mg po bid

Off-Label Uses.

1. Prevention of thromboembolism after orthopedic surgery: 150 mg po bid

MOA. Dabigatran is a competitive, direct thrombin inhibitor. Because thrombin enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of a thrombus. Both free and clot-bound thrombin and thrombin-induced platelet aggregation are inhibited.

Boehringer-Ingelheim
150 mg pictured

Drug Characteristics: Dabigatran

Dose Adjustment Hepatic	Not required	**Absorption**	F = 3-7%, no effect of food on absorption
Dose Adjustment Renal	CrCl 15-30 mL/min, 75 mg po bid; CrCl <15 mL/min, avoid use	**Distribution**	Vd = 50-70 L; 35% protein bound
Dialyzable	Use in ESRD should be avoided; hemodialysis removes 60% of drug in 2-3 h	**Metabolism**	Extensive hepatic metabolism but not by CYP; substrate of P-glycoprotein
Pregnancy Category	C	**Elimination**	Renal elimination is 80% with a half-life of 12-17 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Active bleeding, prosthetic heart valve	**Black Box Warnings**	Use in elderly; risk of stroke at discontinuation; spinal epidural hematoma

Medication Safety Issues: Dabigatran

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not open; F increased 75% when capsule opened	Yes	Plavix	No

Drug Interactions: Dabigatran

Typical Agents	Mechanism	Clinical Management
P-glycoprotein inducers	Increased dabigatran metabolism reduces dabigatran effectiveness	Monitor and consider dose increases of dabigatran
P-glycoprotein inhibitors	Decreased dabigatran metabolism increases risk of dabigatran toxicity	If concurrent P-glycoprotein inhibitor and CrCl 30-50 mL/min, reduce dabigatran dose to 75 mg po bid; avoid concurrent use if CrCl <30 mL/min
Antiplatelet agents, NSAIDs, anticoagulants	Additive risk of bleeding	Avoid concurrent use or monitor carefully and adjust dose if necessary

Adverse Reactions: Dabigatran

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bleeding	Gastritis, GERD	Major bleeding, MI, intracranial hemorrhage

Efficacy Monitoring Parameters. Prevention of clotting or recurrence of clotting. The aPTT assay can be used as a qualitative indicator of anticoagulation status.

Toxicity Monitoring Parameters. Monitor for signs and symptoms of bleeding; evaluate renal function. Not recommended in valvular heart disease.

Key Patient Counseling Points. May be given with or without food. Do not open capsules. Treatment must be suspended prior to surgical procedures, using protocols provided in the product package insert. Increased risk of stroke on discontinuation.

Clinical Pearls. Detailed dosing conversion protocols used to convert patients from warfarin or parenteral anticoagulants to dabigatran are available in the product package insert. Dispense in manufacturer original bottle and discard remaining doses 4 mo after opening. Guidelines recommend against use in advanced liver disease or CrCl <15 mL/min. Medication guide required at dispensing.

DARBEPOETIN: Aranesp

Class: Hematopoietic

Dosage Forms. **Injection Solution, Vial:** 25 mcg/mL, 40 mcg/mL, 60 mcg/mL, 100 mcg/mL, 200 mcg/mL, 300 mcg/mL, 500 mcg/mL; **Injectable Solution, Prefilled Syringe:** 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 150 mcg/0.75 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL

Amgen 100 mcg/0.5 mL pictured

Common FDA Label Indication, Dosing, and Titration.

1. Anemia due to chemotherapy: 2.25 mcg/kg sq weekly; or 500 mcg sq every 3 wk; dose adjusted based on changes in Hgb levels
2. Anemia of chronic kidney disease: Patients not on dialysis, 0.45 mcg/kg IV or sq once every 4 wk; Patients on dialysis 45, mcg/kg IV or sq once weekly or 0.75 mcg/kg IV or sq once every 2 wk; dose adjusted based on changes in Hgb levels

Off-Label Uses.

1. Anemia associated with myelodysplastic syndrome: 150-300 mcg sq weekly

MOA. Darbepoetin alfa is a hyperglycosylated analogue of recombinant human erythropoietin. It binds to the erythropoietin receptor on erythroid progenitor cells, stimulating production/differentiation of mature red cells.

Drug Characteristics: Darbepoetin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 37%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 52 mL/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatically metabolized via galactose receptors
Pregnancy Category	C	**Elimination**	Minimal renal elimination with a half-life of 46 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to darbepoetin, uncontrolled hypertension	**Black Box Warnings**	Increased CV, stroke, mortality risk; cancer recurrence; REMS program

Medication Safety Issues: Darbepoetin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Aricept, dalteparin, epoetin	No

Drug Interactions: **Darbepoetin.** None

Adverse Reactions: Darbepoetin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, hypertension, diarrhea, injection site thrombosis, myalgia, fatigue	Thromboembolism, myocardial infarction	Pure red cell aplasia, immune hypersensitivity, seizures, tumor progression

Efficacy Monitoring Parameters. For anemia, titrate dose to avoid transfusion (usually target is to keep Hgb >9 g/dL) but discontinue if Hgb >10 g/dL. For renal failure, titrate to keep Hgb between 10 and 11 g/dL. Iron studies to ensure adequate iron stores, transferring saturation >20% and ferritin >100 mg/mL.

Toxicity Monitoring Parameters. BP; weight to monitor edema; SCr in renal failure patients; signs and symptoms of thrombosis; cancer progression. Rapid rise in hemoglobin, >1 g/dL >2 wk may increase the risk for cardiovascular events.

Key Patient Counseling Points. Do not shake, dilute, or expose to light. Refrigerate. Do not combine remainders from different syringes; each syringe is for single use. May require several weeks for maximum effect.

Clinical Pearls. Typically administered in hospital infusion and dialysis clinics. In cancer patients with certain tumor types (eg, breast, non-small cell lung, head and neck, etc), epoetin and darbepoetin shortened overall survival, and/or increased risk of tumor progression or recurrence in some clinical studies. Discontinue after the completion of the chemotherapy course and if no response after 8 wk of therapy. Hospitals and health-care professionals who prescribe and/or dispense darbepoetin to patients with cancer must enroll and comply with the ESA (erythropoiesis-stimulating agent) APPRISE oncology program at www.esa-apprise.com. Renal failure patients experienced greater risks for death, stroke, and serious cardiovascular events when administered ESAs to target Hgb levels of 11 g/dL or higher in clinical studies. Not for initial use in children, typically started on erythropoietin and converted to darbepoetin.

DARIFENACIN: Enablex

Class: Urinary Antispasmodic

Dosage Forms. Oral Tablet, Extended Release: 7.5 mg, 15 mg

Common FDA Label Indication, Dosing, and Titration.

1. Overactive bladder: 7.5 mg po daily, may titrate to 15 mg po daily

Off-Label Uses. None

MOA. Darifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

Warner Chilcott 15 mg pictured

D

Drug Characteristics: Darifenacin

Dose Adjustment Hepatic	Child-Pugh B or C, do not exceed 7.5 mg po daily	**Absorption**	F = 15-25%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 163 L
Dialyzable	Unknown	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5; inhibits CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 60% with a half-life of 13-19 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to darifenacin, gastric retention, glaucoma, urinary retention	**Black Box Warnings**	None

Medication Safety Issues: Darifenacin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush or chew	No	Solifenacin	No

Drug Interactions: Darifenacin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased darifenacin metabolism reduces darifenacin effectiveness	Monitor and consider dose increases of darifenacin
CYP3A4/5 inhibitors	Decreased darifenacin metabolism increases risk of darifenacin toxicity	Monitor and consider dose decreases of darifenacin; *max* dose 7.5 mg/d
CYP2D6 substrates	Inhibition of CYP2D6-mediated metabolism can raise concentrations of substrates	Avoid concurrent use or monitor carefully for signs of substrate toxicity
Anticholinergic agents	Additive anticholinergic adverse effects	Avoid concurrent use or monitor carefully for adverse effects

Adverse Reactions: Darifenacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, xerostomia, blurred vision	Abdominal pain, indigestion, urinary retention, dizziness	Angioedema

Efficacy Monitoring Parameters. Resolution of clinical signs of bladder spasticity, incontinence, urinary urgency and frequency.

Toxicity Monitoring Parameters. Severe anticholinergic effects (dry mouth, cognitive impairment, constipation, vision changes).

Key Patient Counseling Points. This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, constipation, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment. Can be taken with or without food.

Clinical Pearls. May note decline in cognitive function, especially in elderly patients.

DESVENLAFAXINE: Pristiq, Various

Class: Serotonin/Norepinephrine Reuptake Inhibitor

Dosage Forms. Oral Tablet, Extended Release: 50 mg, 100 mg

Pfizer 50 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Depression: 50 mg po daily

Off-Label Uses.

1. Menopausal flushing: 100 mg po daily

MOA. Desvenlafaxine is a potent reuptake inhibitor of serotonin and norepinephrine, like many TCAs, but lacks effects on muscarinic, α-adrenergic, or histamine receptors.

Drug Characteristics: Desvenlafaxine

Dose Adjustment Hepatic	Moderate to severe impairment, *max* dose, 100 mg po daily	**Absorption**	F = 80%; no effect of food on absorption
Dose Adjustment Renal	CrCl = 30-50 mL/min, *max* 50 mg po daily; CrCl <30 mL/min, *max* 50 mg po qod	**Distribution**	Vd = 3.4 L/kg; 30% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism via conjugation
Pregnancy Category	C	**Elimination**	Renal elimination is 45% as unchanged drug, with a half-life of 10-11 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to desvenlafaxine or venlafaxine; MAOI use	**Black Box Warnings**	Suicidality; not for use in children; not for bipolar disorder

Medication Safety Issues: Desvenlafaxine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	ER tablets	No	Prilosec	No

Drug Interactions: Desvenlafaxine

Typical Agents	Mechanism	Clinical Management
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Triptans, SSRIs, tramadol	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia)
Linezolid, metoclopramide, MAOI	Increased risk of serotonin syndrome	Concurrent use contraindicated

Adverse Reactions: Desvenlafaxine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diaphoresis, dizziness, headache, nausea, xerostomia	Anxiety, bleeding, blurred vision, constipation, diarrhea, disorder of ejaculation, fatigue, feeling nervous, hypertension, hyponatremia, insomnia, loss of appetite, proteinuria, serum cholesterol raised, sexual dysfunction, somnolence, tremor, vomiting, weight loss	GI hemorrhage, serotonin syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding, monitor BP, LFT, and serum cholesterol levels, in case of severe impairment at baseline and periodically during therapy; signs/symptoms of hyponatremia, especially in patients on concomitant diuretics, volume-depleted patients, and elderly. Monitor renal function.

Key Patient Counseling Points. Take with food, but avoid alcohol. Symptomatic improvement may not be evident for a few weeks. Do not discontinue drug abruptly, as this may precipitate withdrawal symptoms such as dysphoric mood, irritability, and agitation. Avoid activities requiring mental alertness or coordination until drug effects are realized, as this medicine may cause dizziness or somnolence.

Clinical Pearls. Safety and efficacy not established in children. Medication guide required at dispensing.

DEXAMETHASONE ORAL: Decadron, Various

Class: Adrenal Corticosteroid

Dosage Forms. Oral Tablet: 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg; **Oral Solution:** 0.5 mg/5 mL; **Oral Elixir:** 0.5 mg/5 mL

Roxane generic pictured

Common FDA Label Indication, Dosing, and Titration.

Dosing for indications listed below: Adults, 0.75-9 mg/d po; Children, 0.02-0.3 mg/kg/d in 3-4 divided doses; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

Off-Label Uses.

1. Chemotherapy-induced nausea and vomiting: 20 mg IV before chemotherapy, 8 mg IV or po bid × 3 d after chemotherapy

MOA. Glucocorticosteroids are naturally occurring, and synthetic adrenocortical steroids cause varied metabolic effects, modify the body's immune responses to diverse stimuli and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

Drug Characteristics: Dexamethasone Oral

Dose Adjustment Hepatic	Adjust dose to response	**Absorption**	F = 85%
Dose Adjustment Renal	Adjust dose to response	**Distribution**	Vd = 2 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatic; substrate of CYP3A4/5; inhibitor of P-glycoprotein; inducer of CYP3A4/5 and P-glycoprotein
Pregnancy Category	C	**Elimination**	Primarily renal elimination with a half-life of 2-2.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to glucocorticosteroids; concurrent use of live vaccines; fungal infections	**Black Box Warnings**	None

Medication Safety Issues: Dexamethasone Oral

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Methadone	No

Drug Interactions: Dexamethasone Oral

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased dexamethasone metabolism reduces dexamethasone effectiveness	Monitor and consider dose increases of dexamethasone
CYP3A4/5 inhibitors	Decreased dexamethasone metabolism increases risk of dexamethasone toxicity	Monitor and consider dose decreases of dexamethasone
CYP3A4/5 substrates	Induced metabolism of CYP3A4/5 substrates results in increased metabolism and loss of substrate effectiveness	Monitor and consider substrate dose increases
P-glycoprotein substrates	Metabolism of substrates may be inhibited or induced	Monitor and consider substrate dose increase or decrease depending on therapeutic effect
Fluoroquinolones	Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly	Avoid concurrent use, or monitor carefully for tendon rupture
Phenytoin	Phenytoin increases dexamethasone metabolism; dexamethasone can increase or decrease phenytoin metabolism	Monitor dexamethasone efficacy and phenytoin concentrations
Warfarin	Steroids can either increase or decrease INR in patients taking warfarin	Monitor INR carefully

Adverse Reactions: Dexamethasone Oral

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
GI upset	Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia	Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection

Efficacy Monitoring Parameters. Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

Toxicity Monitoring Parameters. Monitor for signs of hyperglycemia, leukocytosis, osteoporosis, and adrenocortical insufficiency and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

Key Patient Counseling Points. For short-term treatment, inform patients to take doses with meals to prevent GI upset. For high dose or longer-term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection. Patient may experience insomnia, anxiety, aggression at higher doses.

Clinical Pearls. Available in a wide variety of dosage forms for various indications, including injectable, topical, otic, and ophthalmic preparations. Use lowest effective and discontinue as soon as possible to avoid serious long-term adverse effects. Use with caution in patient with history of diabetes.

DEXLANSOPRAZOLE: Dexilant

Class: Proton Pump Inhibitor

Dosage Forms. Oral Capsule, Delayed Release: 30 mg, 60 mg

Common FDA Label Indication, Dosing, and Titration.

1. Erosive esophagitis, treatment: 60 mg po daily × 8 wk; thereafter may continue 30 mg po daily × 6 mo
2. Symptomatic gastroesophageal reflux disease: 30 mg po daily × 4 wk

Off-Label Uses. None.

MOA. Lansoprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^+/K^+-ATPase (proton pump), which is the final pathway for acid secretion.

Drug Characteristics: Dexlansoprazole

Dose Adjustment Hepatic	Child-Pugh class B: *max* 30 mg po daily; Child-Pugh class C: avoid.	**Absorption**	Well absorbed after oral administration
Dose Adjustment Renal	Not required	**Distribution**	Vd = 40.3 L; 96-99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic by multiple pathways including CYP2C19 and CYP3A4/5, but CYP inhibitors/inducers do not produce clinically relevant interactions
Pregnancy Category	B	**Elimination**	Renal elimination is 50.7%; fecal 47.6% with a half-life of 1-2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None
Contraindications	Hypersensitivity to dexlansoprazole or other PPI	**Black Box Warnings**	None

Medication Safety Issues: Dexlansoprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	If capsules are opened, granules should not be chewed	No	Aripiprazole, lansoprazole	No

Drug Interactions: Dexlansoprazole

Typical Agents	Mechanism	Clinical Management
pH-dependent drugs	As lansoprazole lowers gastric pH, absorption of drugs that require acid environment is reduced	Avoid concurrent use

Adverse Reactions: Dexlansoprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, abdominal pain, nausea, f atulence, vomiting	Stevens-Johnson syndrome, rhabdomyolysis, acute interstitial nephritis, *C. diff cile* diarrhea, hypomagnesemia, myocardial infarction

Efficacy Monitoring Parameters. Resolution of GI discomfort.

Toxicity Monitoring Parameters. Seek medical attention if severe headache or blistering skin rash occurs. Prolonged duration of therapy may increase risk of *C. difficile* infection in a hospitalized patient.

Key Patient Counseling Points. May be taken without regard to meals. Should not be taken with antacids.

Clinical Pearls. Other PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of bone fracture with long-term use, use with caution in those with osteoporosis. Medication guide required at dispensing. Unlike lansoprazole, does not interact with clopidogrel or CYP inhibitors/inducers.

DEXMETHYLPHENIDATE: Focalin, Various

Class: CNS Stimulant. C-II

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg; **Oral Capsule, Extended Release:** 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Attention-deficit hyperactivity disorder, methylphenidate-naive patients: Adults, immediate release 2.5 mg po bid (*max* 20 mg po daily) or extended release 10 mg po daily (*max* of 40 mg/d); Children ≥ 6 y of age, immediate release 2.5 mg po bid (*max* 20 mg po daily) or extended release 5 mg po daily (*max* of 30 mg/d)
2. Attention-deficit hyperactivity disorder currently using methylphenidate: Adults and Children ≥ 6 y of age, one-half the total daily dose of extended-release racemic methylphenidate; patients currently using dexmethylphenidate immediate release may be switched to the same daily dose of dexmethylphenidate extended release

Novartis pictured

Off-Label Uses. None

MOA. Amphetamines are noncatecholamine sympathomimetic amines with CNS stimulant activity. Amphetamines are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

Drug Characteristics: Dexmethylphenidate

Dose Adjustment Hepatic	Not required	**Absorption**	F = 22-25%, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.6 L/kg
Dialyzable	Unknown	**Metabolism**	Extensive via de-esterification
Pregnancy Category	C	**Elimination**	Minimal renal elimination with a half-life of 3 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to amphetamines, MAOI use, drug dependence, glaucoma, tics, or history of Tourette syndrome	**Black Box Warnings**	Tolerance and dependence; risk of psychosis

Medication Safety Issues: Dexmethylphenidate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	No	Extended-release capsule, but may open	No	Methadone, Folotyn	No

Drug Interactions: Dexmethylphenidate

Typical Agents	Mechanism	Clinical Management
TCAs	Enhanced amphetamine effects from the release of norepinephrine (hypertension, CNS stimulation)	Avoid concurrent use
MAOIs	Hypertensive crisis	Contraindicated within 14 d

Adverse Reactions: Dexmethylphenidate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight loss, loss of appetite, headache, insomnia, restlessness	Anxiety, tachycardia	Seizures, spasmodic movement, anemia, thrombocytopenia, psychosis, mania, drug dependence, priapism

Efficacy Monitoring Parameters. Resolution of signs of ADHD (improved attention span and reduced impulsivity).

Toxicity Monitoring Parameters. Monitor BP, HR, weight, CBC. Seek medical attention if chest pain, seizures, heart palpitations, change in behavior or personality, hostility. Growth rate in children.

Key Patient Counseling Points. Avoid late evening doses due to resulting insomnia. If you cannot swallow the extended-release capsule, you may open it and pour the medicine into a small amount of soft food such as applesauce. Stir this mixture well and swallow it without chewing.

Clinical Pearls. Dexmethylphenidate is the d-enantiomer of methylphenidate. Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and should be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events.

DIAZEPAM: Valium, Various

Class: Benzodiazepine. C-IV

Dosage Forms. **Oral Tablet:** 2 mg, 5 mg, 10 mg; **Oral Solution:** 1 mg/mL, 5 mg/mL; **Rectal Gel:** 20 mg/5 mL

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Alcohol withdrawal syndrome: 10 mg po tid-qid in first 24 h, then 5 mg po tid-qid prn
2. Anxiety: Adults, 2-10 mg po bid-qid; Children, 1-2.5 mg po tid-qid
3. Seizure, adjunct: Adults, 2-10 mg po bid-qid; Children, 1-2.5 mg po tid-qid

Off-Label Uses.

1. Benzodiazepine withdrawal syndrome: 10 mg po tid-qid in first 24 h, then 5 mg po tid-qid prn

MOA. Enhanced postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA)

Drug Characteristics: Diazepam

Dose Adjustment Hepatic	Decrease dose by 50%	**Absorption**	F = 98%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic; substrate of CYP2C19 and CYP3A4/5
Pregnancy Category	D	**Elimination**	Renal elimination is 75% with a half-life of 24-48 h
Lactation	Avoid	**Pharmacogenetics**	Use with caution in CYP2C19 poor metabolizers
Contraindications	Hypersensitivity to benzodiazepines, narrow-angle glaucoma, severe liver disease, myasthenia gravis, sleep apnea, respiratory insufficiency, children <6 mo	**Black Box Warnings**	None

Medication Safety Issues: Diazepam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	LORazepam	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium.

Drug Interactions: Diazepam

Typical Agents	Mechanism	Clinical Management
Alfentanil, opioids, and other respiratory depressants	Additive respiratory depression	Avoid if possible and consider dose reductions of both agents
CYP2C19, CYP3A4/5 inducers	Increased diazepam metabolism reduces diazepam effectiveness	Monitor and consider dose increases of diazepam
CYP2C19, CYP3A4/5 inhibitors	Decreased diazepam metabolism increases risk of diazepam toxicity	Monitor and consider dose decreases of diazepam
Ethinyl estradiol and other estrogen-based birth control products	Inhibition of diazepam metabolism and additional toxicity	Use with caution
Digoxin	Reduced renal clearance of digoxin and increased digoxin toxicity	Monitor digoxin levels and consider dose reductions

Adverse Reactions: Diazepam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Drowsiness, impaired motor coordination	Confusion, ataxia, nausea and vomiting, blurred vision	Seizures, mania, depression, withdrawal symptoms, elevated liver function tests

Efficacy Monitoring Parameters. Reduction in anxiety symptoms, alcohol withdrawal symptoms, or seizures.

Toxicity Monitoring Parameters. Severe drowsiness, thoughts of suicide, yellowing of eyes, seizures.

Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

Clinical Pearls. Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants concurrently with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. Long-acting benzodiazepines have increased risk of physical and psychological dependence when compared to short acting.

DICLOFENAC: Voltaren, Various

Class: NSAID

Dosage Forms. **Oral Tablet:** 50 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 75 mg, 100 mg; **Oral Capsule:** 18 mg, 25 mg, 35 mg; **Powder for Oral Solution:** 50 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Pain: Immediate-release tablet or capsule only, 18-50 mg po tid
2. Dysmenorrhea: Immediate-release tablets only, 50 mg po tid
3. Migraine: Powder for solution only, 50 mg po once
4. Osteoarthritis: 100 mg extended release po daily or bid
5. Rheumatoid arthritis: 100 mg extended release daily or bid

Off-Label Uses. None

MOA. Nonselective inhibitor of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2)

Drug Characteristics: Diclofenac

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50%, minimal food effect
Dose Adjustment Renal	CrCl <30 mL/min, avoid use	**Distribution**	Vd = 1.3 L/kg
Dialyzable	Unknown	**Metabolism**	Hepatic; minor substrate of multiple CYP pathways
Pregnancy Category	C, <30 wk gestation; D, ≥30 wk gestation	**Elimination**	Renal elimination is 65% with a half-life of 2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to diclofenac, concurrent ketorolac, pentoxifylline use, asthma, allergic-type reaction following other NSAID use, CABG	**Black Box Warnings**	Cardiovascular, GI risk, CABG

Medication Safety Issues: Diclofenac

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	No	XR should not be crushed	No	Diflucan	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent.

Drug Interactions: Diclofenac

Typical Agents	Mechanism	Clinical Management
Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline	Additive GI toxicity and increased risk of bleeding	Concurrent ketorolac, pentoxifylline contraindicated; others, monitor for GI toxicity
ACEIs, ARBs, beta-blockers, loop and thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
Cholestyramine	Decreased absorption of diclofenac	Separate administration by 1-2 h
Most CYP inducers	Increased diclofenac metabolism reduces diclofenac effectiveness	Consider dose increases of diclofenac
Most CYP inhibitors	Decreased diclofenac metabolism increases risk of diclofenac toxicity	Consider dose decreases of diclofenac
Cyclosporine, tacrolimus	Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism	Monitor cyclosporine and tacrolimus levels and consider dose adjustments
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid concurrent use in patients with renal dysfunction
Sulfonylureas	Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism	Monitor FPG and adjust as necessary
Warfarin	Both substrates for CYP2C9, competitive metabolism	Monitor INR and adjust warfarin dose

Adverse Reactions: Diclofenac

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headaches, GI distress	GI ulcers	Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, myocardial infarction, aplastic anemia, hemolytic anemia

Efficacy Monitoring Parameters. Decreased pain and improved range of motion.

Toxicity Monitoring Parameters. Monitor CBC, LFTs, SCr, fecal occult blood tests, severe skin rash, black tarry stools, chest pain, yellowing of eyes or skin, and change in urination.

Key Patient Counseling Points. Take with food or milk to decrease GI upset.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk of cardiovascular effects. Use lowest dose for shortest period of time to minimize toxicity. Available in both sodium and potassium salts, in combination with misoprostol, and in ophthalmic and topical products. Medication guide required at dispensing.

DICYCLOMINE: Bentyl, Various

Class: Antimuscarinic

Dosage Forms. **Oral Capsule:** 10 mg; **Oral Tablet:** 20 mg; **Oral Syrup:** 10 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Irritable bowel syndrome: Children 6 mo-2 y of age, 5 mg po tid-qid; Children 2-12 y of age, 10 mg po tid, may titrate to 40 mg/d; Adults, 20 mg po qid, may titrate to 40 mg po qid

Watson generic 20 mg pictured

Mylan generic 10 mg pictured

Off-Label Uses. None

MOA. Dicyclomine relieves smooth muscle spasm of the GI tract via a specific anticholinergic effect (antimuscarinic) at the acetylcholine-receptor sites and a direct effect on smooth muscle (musculotropic).

Drug Characteristics: Dicyclomine

Dose Adjustment Hepatic	Not required	**Absorption**	Well absorbed, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3.65 L/kg
Dialyzable	Unknown	**Metabolism**	Minimal
Pregnancy Category	B	**Elimination**	Renal elimination is 80% with a half-life of 2 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to dicyclomine, age <6 mo, breastfeeding, GI obstruction, glaucoma, myasthenia gravis, obstructive uropathy, ref ux esophagitis, severe ulcerative colitis, toxic megacolon, unstable cardiovascular state in acute hemorrhage	**Black Box Warnings**	None

Medication Safety Issues: Dicyclomine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	DiphenhydrAMINE, doxycycline	Avoid except in short-term palliative care to decrease oral secretions. Highly anticholinergic, uncertain effectiveness.

Drug Interactions: Dicyclomine

Typical Agents	Mechanism	Clinical Management
Agents with anticholinergic effects	Additive anticholinergic adverse effects can result	Avoid concurrent use or monitor carefully for adverse effects

Adverse Reactions: Dicyclomine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Decreased sweating, xerostomia, GI distress, blurred vision, dizziness, constipation, drowsiness	Tachycardia, urinary retention	Psychosis, euphoria, anaphylaxis, drug dependence

Efficacy Monitoring Parameters. Improved bowel function, decreased flatulence, diarrhea.

Toxicity Monitoring Parameters. Rapid heart beat, severe dizziness, unusual thoughts, shortness of breath, or severe rash.

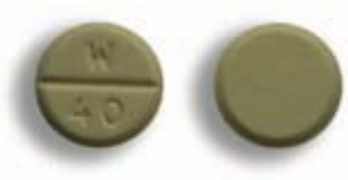
Key Patient Counseling Points. May cause drowsiness; avoid driving and operating heavy equipment. Heat prostration (due to decreased sweating) can occur when used in a hot environment.

Clinical Pearls. There are reports that administration of dicyclomine to infants has been followed by serious respiratory symptoms (dyspnea, shortness of breath, breathlessness, respiratory collapse, apnea, asphyxia), seizures, syncope, pulse rate fluctuations, muscular hypotonia, and coma. Death has been reported.

DIGOXIN: Lanoxin, Various

Class: Digitalis Glycoside

Dosage Forms. **Oral Tablet:** 62.5 mcg, 125 mcg, 187.5 mcg, 250 mcg; **Oral Solution:** 0.05 mg/mL



West-ward generic 0.125 mg pictured

Jerome Stevens Pharmaceuticals generic 0.25 mg pictured

D

Common FDA Label Indication, Dosing, and Titration.

1. Atrial fibrillation: Loading dose of 0.25 mg po q2h to a total dose of 1.5 mg, then 0.125-0.375 mg po daily
2. Heart failure: Premature infant, loading dose of 20 mcg/kg, then 5 mcg/kg/d; Full-term infant to children 2 mo of age, loading dose of 30 mcg/kg, then 8-10 mcg/kg/d; Children 2-23 mo of age, loading dose of 40-50 mcg/kg, then 10-12 mcg/kg/d; Children 2-10 y of age, loading dose of 30-40 mcg/kg (solution), then 8-10 mcg/kg/d; Children >10 y of age, loading dose of 0.75-1.5 mg/kg, then 0.125-0.5 mg/kg po; Adults, loading dose of 0.5-0.75 mg po once, followed by 0.125-0.375 mg po q6-8h to achieve response, followed by 0.125-0.5 mg po daily
3. Supraventricular tachyarrhythmia: Loading dose of 0.75-1.5 mg po (divided into 3 doses, ½ of total dose initially, followed by ¼ of total dose at 6-8 h intervals later), then 0.125-0.5 mg po daily

Off-Label Uses.

1. Fetal tachycardia, supraventricular tachycardia: 0.125-0.375 mg po daily (administered to mother)

MOA. Digitalis glycosides exert positive inotropic effects through improved availability of calcium to myocardial contractile elements, thereby increasing cardiac output in heart failure. Antiarrhythmic actions are caused primarily by an increase in AV nodal refractory period via increased vagal tone, sympathetic withdrawal, and direct mechanisms.

Drug Characteristics: Digoxin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60-80% (tablet); food reduces absorption rate
Dose Adjustment Renal	Mild-to-moderate renal impairment, 0.125 mg po daily; severe renal impairment, 0.0625 mg po daily; titrate q2wk	**Distribution**	Vd = 4-7 L/kg; 25% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Modest hepatic; substrate of P-glycoprotein
Pregnancy Category	C	**Elimination**	Renal elimination (unchanged) is 57-80% with a half-life of 1.3-2.2 d
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to digoxin, ventricular fibrillation	**Black Box Warnings**	None

Medication Safety Issues: Digoxin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Desoxyn, doxepin	Avoid >0.125 mg/d. In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity.

Drug Interactions: Digoxin

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Increased risk of bradycardia and AV block	Monitor heart rate and ECG
Diuretics	Increased risk of digoxin toxicity due to potassium depletion	Monitor potassium and supplement if necessary
P-glycoprotein inducers	Increased digoxin metabolism reduces digoxin effectiveness	Monitor and consider dose increases of digoxin
P-glycoprotein inhibitors	Decreased digoxin metabolism increases risk of digoxin toxicity	Monitor and consider dose decreases of digoxin
Antacids, bile acid sequestrants, sucralfate	Decreased digoxin absorption and decreased efficacy	Avoid concurrent use or give digoxin 1-2 h before medications that decrease absorption

Adverse Reactions: Digoxin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Anorexia, confusion, diarrhea, dizziness, ECG changes, headache, nausea, rash, reduced color discrimination, visual disturbances, vomiting, weakness	Cardiac dysrhythmias, psychosis, seizures

Efficacy Monitoring Parameters. ECG, decreased heart rate, improvement in signs/symptoms of heart failure; therapeutic serum range 0.8-2 ng/mL.

Toxicity Monitoring Parameters. ECG for cardiac dysrhythmia, excessive bradycardia; SCr, and serum electrolytes (especially potassium, magnesium, calcium).

Key Patient Counseling Points. Take after morning meals (and after evening meals if giving in divided doses). Report signs/symptoms of bradycardia. Do not discontinue drug suddenly.

Clinical Pearls. Tablet and solution not interchangeable—dosing varies with dosage form. Use with caution in elderly.

DILTIAZEM: Cardizem, Various

Class: Calcium Channel Blocker

Dosage Forms. **Oral Tablet:** 30 mg, 60 mg, 90 mg, 120 mg; **Oral Capsule, Extended Release, 12 h:** 60 mg, 90 mg, 120 mg; **Oral Capsule, Extended Release, 24 h:** 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, 420 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Extended release, 12 h, 60-120 mg po bid, may titrate to 360 mg/d po; Extended release, 24 h, 120-240 mg po daily, may titrate to 540 mg po daily
2. Stable, chronic angina: Immediate release, 30 mg po qid, may titrate to 360 mg/d po; Extended release, 24 h, 120 mg po daily, may titrate to 540 mg/d po

Off-Label Uses.

1. Atrial arrhythmia: 180-360 mg daily po
2. Hypertension: Children, 1.5-2 mg/kg/d po in 3-4 divided doses, may titrate to 3.5 mg/kg/d po

MOA. Diltiazem is a calcium-channel-blocking drug that decreases heart rate, prolongs AV nodal conduction, and decreases arteriolar and coronary vascular tone. It also has negative inotropic properties.

Mylan generic
180 mg pictured

Mylan generic
240 mg pictured

Teva generic
300 mg pictured

D

Drug Characteristics: Diltiazem

Dose Adjustment Hepatic	Dosage reduction may be needed	**Absorption**	F = 35-40% immediate release, F = 93-95% extended release; food decreases absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 305-391 L; 77-93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5. P-glycoprotein; moderate inhibitor of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 35% with a half-life of 3-6.6 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to diltiazem; hypotension; 2nd- or 3rd-degree AV block, sick sinus syndrome	**Black Box Warnings**	None

Medication Safety Issues: Diltiazem

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Cardizem CR, Cardizem LA	No	Extended-release formulations	Yes	Cardene	No

Drug Interactions: Diltiazem

Typical Agents	Mechanism	Clinical Management
CYP3A4/5, P-glycoprotein inducers	Increased diltiazem metabolism reduces diltiazem effectiveness	Monitor and consider dose increases of diltiazem
CYP3A4/5, P-glycoprotein inhibitors	Decreased diltiazem metabolism increases risk of diltiazem toxicity	Monitor and consider dose decreases of diltiazem
CYP3A4/5 substrates	Decreased metabolism and increased toxicity of CYP3A4/5 substrates	Avoid sensitive CYP3A4/5 substrates
Beta-blockers	Increased risk of hypotension, bradycardia, AV conduction disturbances	Avoid concurrent use or monitor BP and heart rate

Adverse Reactions: Diltiazem

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, headache	Bradycardia, constipation, dizziness, fatigue, headache, hypotension, rash, syncope	Heart failure, heart block, hepatotoxicity

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of angina attacks, reduction in use of nitroglycerin for chest pain.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased heart rate, signs/symptoms of liver toxicity; exacerbations of angina pectoris or acute coronary insufficiency while tapering chronic therapy, especially in patients with CAD.

Key Patient Counseling Points. Report symptomatic hypotension, bradyarrhythmia, peripheral edema, or syncope. This drug is available in multiple brand names with varying properties by brand. Instruct patient to follow administration instructions specific to the prescribed brand with regards to meals and timing. Do not drink alcohol while taking this drug.

Clinical Pearls. Patient should avoid concomitant use of beta-blockers during drug therapy, unless otherwise directed by health-care professional.

DIPHENOXYLATE/ATROPINE: Lomotil, Various

Class: Antidiarrheal. C-V

Dosage Forms. Oral Tablet: Diphenoxylate 2.5 mg with atropine 0.025 mg; **Oral Solution:** Diphenoxylate 2.5 mg/5 mL with atropine 0.025 mg/5 mL

Mylan generic 2.5 mg/0.025 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Diarrhea: Children ≥ 2 y of age, 0.3 mg-0.4 mg/kg/d (diphenoxylate) po qid to *max* of 20 mg/d (diphenoxylate); Adults, 2 tablets po qid until diarrhea resolves, then reduce dose to maintain efficacy, to *max* of 20 mg/d (diphenoxylate)

Off-Label Uses. None

MOA. Diphenoxylate is a synthetic meperidine congener without analgesic activity that slows GI motility. Because high doses of diphenoxylate (40-60 mg) cause systemic opioid activity, atropine is added in subtherapeutic amounts to decrease abuse potential.

Drug Characteristics: Diphenoxylate/Atropine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 324 L
Dialyzable	Not dialyzable	**Metabolism**	Rapidly and extensively hepatically metabolized to an active metabolite
Pregnancy Category	C	**Elimination**	Renal elimination is 14% with half-life of 2.5 h for parent compound and 12-14 h for active metabolite
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to diphenoxylate or atropine products; diarrhea associated with enterotoxin-producing bacteria or pseudomembranous enterocolitis; obstructive jaundice	**Black Box Warnings**	None

Medication Safety Issues: Diphenoxylate/Atropine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	LaMICtal, LamISIL, loperamide	No

Drug Interactions: Diphenoxylate/Atropine

Typical Agents	Mechanism	Clinical Management
Agents with anticholinergic effects	Additive anticholinergic adverse effects can result	Avoid concurrent use or monitor carefully for adverse effects
MAOI	Increased risk of serotonin syndrome	Avoid concurrent use

Adverse Reactions: Diphenoxylate/Atropine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Abdominal discomfort, nausea and vomiting	Dizziness, sedation, somnolence, malaise, dry mouth	Pancreatitis, toxic megacolon, anaphylaxis

Efficacy Monitoring Parameters. Frequency and volume of bowel movements; body temperature; blood in stool.

Toxicity Monitoring Parameters. Monitor for signs of atropine toxicity and for abdominal distention.

Key Patient Counseling Points. This drug can cause dry mouth, blurred vision, drowsiness, or dizziness; use caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. Avoid alcohol and other CNS depressants. Seek medical attention if diarrhea persists or if fever, palpitations, or abdominal distention occurs. Ensure *max* daily dose is not exceeded to avoid toxicity.

Clinical Pearls. Signs of atropine toxicity often referred to as "dry as a bone, hot as a hare, red as a beet, blind as a bat, mad as a hatter." Higher than usual doses may be administered to patients receiving irinotecan.

DIPHTHERIA TOXOID: Daptacel, Adacel, Boostrix

Class: Vaccine

Dosage Forms. **Suspension for Intramuscular Injection:** For adults, available in combination with tetanus and acellular pertussis (Tdap); for children, available in combination with tetanus and acellular pertussis (DTaP), and in combinattion with other pediatric vaccines

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of diphtheria: Children, all infants at age 2, 4, 6, and 12-15 mo, and a 5th dose at age 4-6 y, as primary series of DTaP; Tdap at age 11-12 y; single dose of Tdap for all adults at next opportunity; Td every 10 y for adults

Off-Label Uses. None

Drug Characteristics: Diphtheria Toxoid

Pregnancy Category	C	**ADME**	Not known
Lactation	Caution advised; weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to diphtheria toxoid or a component of the vaccine	**Black Box Warnings**	None

Medication Safety Issues: Diphtheria Toxoid

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Adacel, Daptacel	No

Infanrix GlaxoSmithKline pictured

D

Drug Interactions: Diphtheria Toxoid

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression	Delay diphtheria toxoid administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents	Immunosuppression	Delay diphtheria administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: Diphtheria Toxoid

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb	GI symptoms	Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of diphtheria, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

Toxicity Monitoring Parameters. Monitor for syncope, fever after administration.

Key Patient Counseling Points. Return to provider for each dose in the series.

Clinical Pearls. Use the same brand of vaccine to complete the entire series, if possible.

DIPYRIDAMOLE: Persantine, Various

Class: Platelet Aggregation Inhibitor

Dosage Forms. **Oral Tablet:** 25 mg, 50 mg, 75 mg

Common FDA Label Indication, Dosing, and Titration.

1. Thromboprophylaxis after heart valve replacement: 75-100 mg po qid as an adjunct to warfarin therapy

Off-Label Uses. None

MOA. Inhibits the uptake of adenosine into platelets, endothelial cells, and erythrocytes resulting in an increase in local concentrations of adenosine, which is a coronary vasodilator and a platelet aggregation inhibitor.

Barr Labs generic 75 mg pictured

Drug Characteristics: Dipyridamole

Dose Adjustment Hepatic	Not required	**Absorption**	F = 27-66%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.43-3.38 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensively metabolized but not by CYP; inhibits P-glycoprotein
Pregnancy Category	B	**Elimination**	Eliminated in bile, with a half-life of 10 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to dipyridamole	**Black Box Warnings**	None

Medication Safety Issues: Dipyridamole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Periactin, disopyramide	Avoid oral. May cause orthostatic hypotension.

Drug Interactions: Dipyridamole

Typical Agents	Mechanism	Clinical Management
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Avoid concurrent use
SSRIs, SNRIs	Increased risk of bleeding	Monitor for signs/symptoms of bleeding
P-glycoprotein substrates	Inhibits metabolism of substrates and may result in substrate toxicity	Monitor and consider substrate dose reduction

Adverse Reactions: Dipyridamole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness	Abdominal pain, diarrhea, headache	Ventricular arrhythmia, bronchospasm

Efficacy Monitoring Parameters. Prevention of AMI, stroke, other thrombotic complications.

Toxicity Monitoring Parameters. Signs/symptoms of dizziness, GI distress.

Key Patient Counseling Points. Rise slowly from a sitting/supine position. Avoid alcohol.

Clinical Pearls. Safety and effectiveness in pediatric patients have not been studied. Injectable product also available for radionuclide cardiac perfusion studies. Oral combination product with dipyridamole and aspirin also available. Use with caution in the elderly.

DIVALPROEX: Depakote, Various

Class: Anticonvulsant

Dosage Forms. **Oral Capsule, Extended Release:** 125 mg; **Oral Tablet, Extended Release:** 125 mg, 250 mg, 500 mg; **Oral Capsule, Sprinkles:** 125 mg

Northstar Rx generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Absence seizure, simple and complex: 15 mg/kg/d po, may titrate to 60 mg/kg/d
2. Complex partial epileptic seizure: 10-15 mg/kg/d po, may titrate to 60 mg/kg/d
3. Manic bipolar disorder: 25 mg/kg/d po, may titrate to 60 mg/kg/d
4. Migraine prophylaxis: 500 mg po daily for 1 wk, then 1000 mg po daily

Off-Label Uses. None

MOA. Divalproex is composed of sodium valproate and valproic acid. Valproic acid is a carboxylic acid compound whose anticonvulsant activity might be mediated by an inhibitory neurotransmitter, GABA. Valproic acid might increase GABA levels by inhibiting GABA metabolism or enhancing post-synaptic GABA activity. Valproic acid also limits repetitive neuronal firing through voltage- and usage-dependent sodium channels.

Drug Characteristics: Divalproex

Dose Adjustment Hepatic	Avoid use in severe hepatic dysfunction	**Absorption**	F = 89%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 11 L; 88-90% protein bound
Dialyzable	Yes, but no dosage supplementation required	**Metabolism**	Extensive hepatic metabolism; minor substrate of multiple CYP pathways
Pregnancy Category	X for migraine prophylaxis; D for all other indications	**Elimination**	Renal elimination is 30-50% with a half-life of 9-16 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to divalproex, hepatic disease, urea cycle disorders	**Black Box Warnings**	Hepatotoxicity, teratogenicity, pancreatitis

Medication Safety Issues: Divalproex

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Depakote ER	No	Extended release	No	Depakene	No

Drug Interactions: Divalproex

Typical Agents	Mechanism	Clinical Management
Aspirin, macrolides	Increased valproic acid concentrations and risk of side effects	Monitor valproic acid levels
Carbamazepine, lamotrigine, TCAs	Divalproex inhibits metabolism of these drugs, increasing the risk of toxicity	Monitor for side effects and serum levels if available
Acyclovir, carbapenems, protease inhibitors, rifampin, risperidone	Decreased valproic acid concentrations and loss of anticonvulsant effect	Avoid concomitant use, monitor valproic acid levels
Phenytoin, phenobarbital	Altered levels of these and valproic acid levels	Monitor valproic acid levels and levels of other agents
Olanzapine, oxcarbazepine	Decreased olanzapine or oxcarbazepine concentrations	Monitor for efficacy
Warfarin	Warfarin displaced from protein binding, increasing warfarin effect	Monitor INR

Adverse Reactions: Divalproex

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Abdominal pain, alopecia, asthenia, diarrhea, diplopia, dizziness, headache, nausea, somnolence, tremor, vomiting	Amblyopia, blurred vision, feeling nervous, hyperammonemia, indigestion, infection, insomnia, loss of appetite	Hepatitis, palpitation, pancreatitis, tachycardia, thrombocytopenia

Efficacy Monitoring Parameters. Reduction in number of seizures or control of manic symptoms. Therapeutic range for epilepsy, 50-100 mcg/mL. Therapeutic range for acute mania, 50-125 mcg/mL.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema, increased heart rate, pancreatitis (abdominal pain, nausea, vomiting), monitor LFTs, ammonia levels, and CBC; emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior.

Key Patient Counseling Points. Avoid activities requiring mental alertness until drug effects are realized; drug may cause somnolence or dizziness. Take with food to avoid GI irritation. Do not discontinue drug abruptly, as this may precipitate status epilepticus. Avoid alcohol.

Clinical Pearls. Safety and efficacy in children <10 y of age have not been established. To convert from valproic acid to divalproex, initiate divalproex at the same daily dose and schedule; once stabilized, give divalproex bid or tid. Divalproex can produce teratogenic effects, so use with caution in women of childbearing potential. Multiple other dosage forms available as valproic acid.

DONEPEZIL: Aricept, Aricept ODT, Various

Class: Cholinesterase Inhibitor

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg, 23 mg; **Oral Disintegrating Tablet:** 5 mg, 10 mg

Pfizer pictured

Common FDA Label Indication, Dosing, and Titration.

1. Alzheimer disease, dementia (mild-moderate): 5 mg po daily hs, may titrate to *max* of 10 mg/d
2. Alzheimer disease, dementia (moderate-severe): 5 mg po daily qhs, may titrate to 10 mg/d at 4-6 wk to *max* of 23 mg/d (immediate-release tablet) or 10 mg/d (disintegrating tablet)

Off-Label Uses.

1. Multi-infarct dementia: 5-10 mg po daily hs

MOA. Donepezil enhances the action of acetylcholine by reversibly inhibiting acetylcholinesterase (AChE), the enzyme responsible for its hydrolysis. It has a high degree of selectivity for AChE in the CNS, which might explain the relative lack of peripheral side effects.

Drug Characteristics: Donepezil

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 12 L/kg; 96% protein bound
Dialyzable	Unknown	**Metabolism**	Extensive hepatic; minor substrate of CYP3A4/5 and CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 57% with a half-life of 70 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to donepezil or piperidine derivatives	**Black Box Warnings**	None

Medication Safety Issues: Donepezil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ODT	No	Disintegrating tablet, 23-mg tablet	No	AcipHex	No

Drug Interactions: Donepezil

Typical Agents	Mechanism	Clinical Management
Tolterodine, oxybutynin	Decreased efficacy of donepezil via cholinergic receptor antagonism by anticholinergic drugs	Avoid concurrent use
Ramelteon	Increased ramelteon exposure	Monitor for ramelteon toxicity and consider dose reduction

Adverse Reactions: Donepezil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Asthenia, muscle cramps, depression, diarrhea, dizziness, dream disorder, ecchymosis, fatigue, headache, hypertension, insomnia, loss of appetite, nausea, syncope, urinary incontinence, vomiting, weight loss, peripheral edema	Atrioventricular block, GI bleeding, torsades de pointes

Efficacy Monitoring Parameters. Improvement in symptoms of Alzheimer-type dementia.

Toxicity Monitoring Parameters. Symptoms of active or occult GI bleeding, particularly if patient has history of ulcer disease or is receiving concomitant NSAIDs.

Key Patient Counseling Points. Take at bedtime, with or without food. Allow disintegrating tablet to dissolve on tongue and follow with a glass of water. Adverse effects may be more frequent at dose escalation and tend to resolve with continued use. Report signs/symptoms of GI bleeding.

Clinical Pearls. Safety and effectiveness not established in children. No evidence suggests that donepezil alters the course of Alzheimer disease.

DOXAZOSIN: Cardura, Cardura XL, Various

Teva generic pictured

Class: α_1-Adrenergic Blocker

Dosage Forms. Oral Tablet: 1 mg, 2 mg, 4 mg, 8 mg; **Oral Tablet, Extended Release:** 4 mg, 8 mg

Common FDA Label Indication, Dosing, and Titration.

1. Benign prostatic hyperplasia: Immediate release, 1 mg po daily, may titrate to 1-8 mg po daily; Extended release, 4 mg po daily, may titrate to 8 mg po daily
2. Hypertension: Immediate release, 1 mg po daily, *max* 16 mg po daily

Off-Label Uses.

1. Expulsion of distal ureteral stone: Immediate release, 4 mg po daily in evening

MOA. Doxazosin selectively blocks postsynaptic α_1-adrenergic receptors, reducing peripheral resistance through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic α_2-receptor blockade. Increase urine flow by relaxing smooth muscle tone in the bladder neck and prostate.

Drug Characteristics: Doxazosin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 65%, food increases AUC and Cmax of extended-release product
Dose Adjustment Renal	Not required	**Distribution**	98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 9%, fecal 63%, with a half-life of 22 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to doxazosin or other quinazolines	**Black Box Warnings**	None

Medication Safety Issues: Doxazosin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	No	Extended-release tablet	No	Cardene, Cordarone, doxepin, DOXOrubicin	Avoid use as an antihypertensive. High risk of orthostatic hypotension.

Drug Interactions: Doxazosin

Typical Agents	Mechanism	Clinical Management
Beta-blockers, nifedipine, PDE inhibitors	Increased risk of hypotension, especially with 1st dose of doxazosin	Monitor blood pressure
CYP3A4/5 inducers	Increased doxazosin metabolism reduces doxazosin efficacy	Monitor and consider dose increases of doxazosin
CYP3A4/5 inhibitors	Decreased doxazosin metabolism increases risk of doxazosin toxicity	Monitor and consider dose decreases of doxazosin

Adverse Reactions: Doxazosin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Asthenia, dizziness, edema, fatigue, headache, hypotension, nausea, somnolence, vertigo	Hepatotoxicity, priapism

Efficacy Monitoring Parameters. Decreased BP, improvement in urinary symptoms.

Toxicity Monitoring Parameters. Signs of hypotension, increased HR.

Key Patient Counseling Points. Initial dose should be taken with breakfast. Avoid activities requiring coordination until drug effects are realized, as drug may cause vertigo or dizziness. Rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. Syncope or loss of consciousness is possible with 1st dose or dose increases, especially if patient is in an upright position.

Clinical Pearls. Safety and effectiveness not established in children.

DOXEPIN: Sinequan, Various

Class: Tricyclic Antidepressant

Dosage Forms. Oral Capsule: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg; **Oral Tablet:** 3 mg, 6 mg; **Oral Solution:** 10 mg/mL

25 mg

50 mg

100 mg

Mylan generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Depression, anxiety, alcoholism: Very mild, 25-50 mg po daily, may titrate to 300 mg po daily; Mild-moderate, 75 mg po daily, may titrate to 300 mg po daily
2. Insomnia: Adults <65 y of age, 6 mg po daily hs; Adults ≥65 y of age, 3 mg po daily hs, may titrate to 6 mg po daily hs

Off-Label Uses. None

MOA. Doxepin is a tricyclic antidepressant, which influences the adrenergic activity at the synapses where it prevents norepinephrine deactivation through reuptake into the nerve terminals. By binding to histamine receptor sites, it competitively inhibits the biological activation of histamine receptors. Antagonism of the H_1 receptor is the most likely mechanism by which doxepin exerts its sleep maintenance effect.

Drug Characteristics: Doxepin

Dose Adjustment Hepatic	Not required	**Absorption**	Food increases AUC and Cmax
Dose Adjustment Renal	Not required	**Distribution**	Vd = 20.2 L/kg; 80% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; major substrate of CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination with a half-life of 15 h
Lactation	Avoid	**Pharmacogenetics**	Caution with CYP2D6 poor metabolizers
Contraindications	Hypersensitivity to doxepin; MAOI use, glaucoma, severe urinary retention	**Black Box Warnings**	Suicidality

Medication Safety Issues: Doxepin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	SINEquan	No	No	SEROquel, doxazosin, digoxin	Avoid >6 mg/d. Highly anticholinergic, sedating, and cause orthostatic hypotension.

Drug Interactions: Doxepin

Typical Agents	Mechanism	Clinical Management
MAOIs	Increased risk of serotonin syndrome	Concurrent use contraindicated
Anticholinergics	Increased risk of additive anticholinergic side effects	Monitor for adverse effects
Agents that prolong QT interval	Increased risk of cardiotoxicity	Avoid concurrent use
SSRIs	Increased doxepin concentration and risk of serotonin syndrome	Use caution with concomitant therapy
CYP2D6 inhibitors	Decreased doxepin metabolism increases risk of doxepin toxicity	Monitor and consider dose decreases of doxepin

Adverse Reactions: Doxepin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Xerostomia	Blurred vision, confusion, constipation, dizziness, edema, fatigue, headache, nausea, sexual dysfunction, somnolence, rash, urinary retention, weight gain	Cardiac dysrhythmia, hepatotoxicity, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in depression (depressed mood, suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Change in ECG, monitor LFTs.

Key Patient Counseling Points. Avoid activities requiring mental alertness until drug effects are realized. Symptomatic improvement in depression may not be seen for a few weeks. Avoid abrupt discontinuation of drug. Do not drink alcohol.

Clinical Pearls. Safety and effectiveness not established in children. Also available in topical formulation for pruritus due to atopic dermatitis.

DOXYCYCLINE: Vibramycin, Various

Class: Tetracycline Antibiotic

Dosage Forms. **Powder for Oral Suspension:** 25 mg/5 mL; **Oral Tablet:** 20 mg, 50 mg, 75 mg, 100 mg, 150 mg; **Oral Tablet, Delayed Release:** 75 mg, 100 mg, 150 mg; **Oral Capsule:** 50 mg, 75 mg, 100 mg, 150 mg

West-ward generic 100 mg pictured

Mutual Pharmaceutical generic 50 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acinetobacter infection: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily
2. Acne vulgaris: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily or bid
3. Gonorrhea, uncomplicated: 100 mg po bid × 7 d or 300-mg po single dose followed in 1 h by another 300-mg dose
4. Staphylococcal infection of skin: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily

Off-Label Uses.

1. Lyme disease, prophylaxis: 200 mg po as a single dose

MOA. Doxycycline is a broad-spectrum bacteriostatic compound that inhibits protein synthesis at the 30S ribosomal subunit. Activity includes gram-positive, gram-negative, aerobic, and anaerobic bacteria, as well as spirochetes, mycoplasmas, rickettsiae, chlamydiae, and some protozoa. Many bacteria have developed plasmid-mediated resistance.

Drug Characteristics: Doxycycline

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.75 L/kg, 80% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, 50%
Pregnancy Category	C	**Elimination**	Renal elimination is 35-45% with a half-life of 15-24 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to doxycycline or concurrent acitretin	**Black Box Warnings**	None

Medication Safety Issues: Doxycycline

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Delayed release formulation	No	Doxepin, dicyclomine	No

Drug Interactions: Doxycycline

Typical Agents	Mechanism	Clinical Management
Acitretin	Risk of increased intracranial pressure. Mechanism unknown.	Concurrent use contraindicated
Antacids	Decreased absorption via binding	Separate use by 1-2 h
Digoxin	Tetracyclines alter bacterial flora resulting in decreased metabolism of digoxin	Monitor and consider dose adjustments of digoxin
Penicillin	Tetracyclines may interfere with the bactericidal effect of penicillin	Avoid concurrent use

Adverse Reactions: Doxycycline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Photosensitivity, tooth discoloration in children <8 y of age	Nausea, vomiting, diarrhea	Esophageal ulceration, hypersensitivity, hepatotoxicity, renal toxicity, *C. diff cile* colitis, increased intracranial pressure, decreased growth in children

Monitoring Parameters Efficacy. Resolution of symptoms of infection.

Monitoring Parameters Toxicity. Burning or pain in the stomach, extreme headache, bloody diarrhea, tooth darkening.

Key Patient Counseling Points. May take with food that does not contain calcium. Complete full course of therapy. Symptoms should improve within 2-3 d. Wear sunscreen. Administer with 240 mL of water.

Clinical Pearls. May resume normal activities after 24 h of antibiotics if afebrile. Not for use in children <8 y of age (bone and tooth discoloration).

DULOXETINE: Cymbalta, Various

Class: Serotonin/Norepinephrine Reuptake Inhibitor

Dosage Forms. Oral Capsule, Delayed Release: 20 mg, 30 mg, 60 mg

Lilly pictured

Common FDA Label Indication, Dosing, and Titration.

1. Anxiety: 60 mg po daily, may titrate to 120 mg po daily
2. Depression: 20-30 mg po bid, may titrate to 120 mg po daily
3. Diabetic peripheral neuropathy pain, fibromyalgia, musculoskeletal pain: 60 mg po daily, may titrate to 120 mg po daily

Off-Label Uses.

1. Urinary incontinence: 40 mg po bid

MOA. Duloxetine is a selective serotonin and norepinephrine reuptake inhibitor that exerts its antidepressant and pain inhibitory actions by potentiating the serotonergic and noradrenergic activity in the CNS. It has no significant affinity for adrenergic, dopaminergic, cholinergic, opioid, glutamate, or histaminergic receptors in vitro and does not inhibit monoamine oxidase.

Drug Characteristics: Duloxetine

Dose Adjustment Hepatic	Avoid	**Absorption**	F = 30-80%; food slows absorption
Dose Adjustment Renal	Initiate at low dose and titrate slowly; avoid if CrCl <30 mL/min	**Distribution**	Vd = 1640 L; 90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP1A2 and CYP2D6; inhibits CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 8-17 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to duloxetine; MAOI, TCA, linezolid use, uncontrolled glaucoma	**Black Box Warnings**	Suicidality; not approved for children

Medication Safety Issues: Duloxetine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	DULoxetine	No	No	FLUoxetine	No

Drug Interactions: Duloxetine

Typical Agents	Mechanism	Clinical Management
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Triptans, SSRIs, tramadol	Additive serotonergic activity	Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination)
Linezolid, TCAs, MAOIs	Increased risk of serotonin syndrome	Concomitant use contraindicated
CYP2D6 substrates	Duloxetine inhibits CYP2D6, increasing substrate concentrations and toxicity	Avoid concurrent use or monitor for adverse effects
CYP1A2 inducers	Increased duloxetine metabolism and decreased efficacy	Avoid concurrent use or consider duloxetine dose increase
CYP1A2 and 2D6 inhibitors	Decreased duloxetine metabolism and increased toxicity	Avoid concurrent use or consider duloxetine dose decrease

Adverse Reactions: Duloxetine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, nausea	Agitation, anxiety, asthenia, bleeding, constipation, diarrhea, dizziness, diaphoresis, disorder of ejaculation, fatigue, hyponatremia, increased blood pressure, insomnia, loss of appetite, muscle cramps, mydriasis, rash, sexual dysfunction, somnolence, tremor, vomiting, xerostomia	Hepatotoxicity, serotonin syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression, pain, or anxiety.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior; monitor BP, CBC, electrolytes, and LFTs at baseline and periodically during therapy; ocular pressure and mydriasis.

Key Patient Counseling Points. Report withdrawal symptoms (eg, dysphoric mood, irritability, agitation, sensory disturbances), especially during abrupt discontinuation of therapy. Drug may cause hepatotoxicity and increased risk of bleeding (GI, ecchymoses, epistaxis, petechiae). May require 1-4 wk for improvement of depression symptoms. Report worsening depression, suicidal ideation, or unusual changes in behavior, especially at initiation of therapy or with dose changes. Children at higher risk for these effects during the first few months of therapy. Patient should watch for signs/symptoms of bleeding events and hepatotoxicity. Avoid alcohol. Monitor carefully if on concurrent meds that alter coagulation.

Clinical Pearls. Duloxetine not approved for use in children. Doses >60 mg/d have not been shown to provide increased effectiveness and were less well tolerated than the 60 mg/d dose.

DUTASTERIDE: Avodart

Class: 5α-Reductase Inhibitor

Dosage Forms. Oral Capsule: 0.5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Benign prostatic hyperplasia: 0.5 mg po daily

Off-Label Uses.

1. Male pattern alopecia: 0.5 mg po daily

GlaxoSmithKline 0.5 mg pictured

MOA. Dutasteride inhibits the conversion of testosterone to 5α-dihydrotestosterone (DHT) by 5α-reductase, isoform 1 and 2.

Drug Characteristics: Dutasteride

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 300-500 L
Dialyzable	Not known	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5
Pregnancy Category	X	**Elimination**	Renal elimination is <1% with a half-life of 5 wks
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to dutasteride, pregnancy, children	**Black Box Warnings**	None

Medication Safety Issues: Dutasteride

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush	No	No	No

Drug Interactions: Dutasteride

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased dutasteride metabolism reduces dutasteride effectiveness	Consider dose increases of dutasteride
CYP3A4/5 inhibitors	Decreased dutasteride metabolism increases risk of dutasteride toxicity	Consider dose decreases of dutasteride

Adverse Reactions: Dutasteride

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Gynecomastia, impotence, reduced libido, dizziness	Heart failure, angioedema, allergic skin reactions

Efficacy Monitoring Parameters. American Urologic Association (AUA) Symptom Score, decrease in residual urine volume, increased urinary flow, increased hair growth.

Toxicity Monitoring Parameters. Shortness of breath, skin rash, swelling.

Key Patient Counseling Points. Symptoms may not improve for up to 6 mo after starting treatment. Do not donate blood while taking or for 6 mo after stopping dutasteride, as it may be transfused to a pregnant woman. Women who are pregnant or may become pregnant should avoid touching or handling this medicine. This medicine can get into the body through the skin and may prevent development of genitalia in an unborn male baby.

Clinical Pearls. May be combined with the alpha-blocker tamsulosin for the treatment of BPH. Draw baseline PSA before initiating therapy. Note that PSA will decrease by 50% with treatment; double PSA values when assessing for prostate cancer.

EFAVIRENZ: Sustiva

Class: Antiretroviral Agent, Reverse Transcriptase Inhibitor

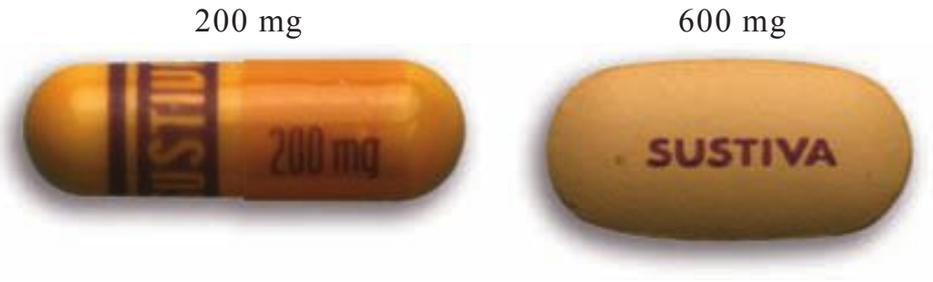
Dosage Forms. Oral Capsule: 50 mg, 200 mg; **Oral Tablet:** 600 mg

Common FDA Label Indication, Dosing, and Titration.

1. Treatment of HIV-1 infections in combination with at least 2 other antiretroviral agents: Adults and Children ≥40 kg, 600 mg po daily; Children <40 kg, weight based and used in combination with ritonavir

Off Label Uses. None

MOA. Binds to HIV reverse transcriptase, blocking the RNA-dependent and DNA-dependent DNA polymerase activities including HIV-1 replication.



Bristol-Myers Squibb pictured

E

Drug Characteristics: Efavirenz

Dose Adjustment Hepatic	Avoid if moderate or severe hepatic impairment	**Absorption**	F = 42%, food increases absorption by 20-30%
Dose Adjustment Renal	Not required	**Distribution**	CSF concentration exceeds serum concentration
Dialyzable	No	**Metabolism**	Hepatic; substrate of via CYP3A/5, 2B6; inhibits CY2C9, and 2C19; induces CYP3A4/5
Pregnancy Category	D	**Elimination**	16-60% unchanged in feces, 14-34% renal as metabolites, with half-life of 52-76 h
Lactation	Avoid	**Pharmacogenetics**	Resistance is associated with HIV mutations
Contraindications	Hypersensitivity or concurrent use of bepridil, cisapride, midazolam, pimozide, triazolam, St. John's wort, or ergot alkaloids	**Black Box Warnings**	None

Medication Safety Issues: Efavirenz

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not open, crush, or chew capsule	Yes	No	No

Drug Interactions: Efavirenz

Typical Agents	Mechanism	Clinical Management
Boceprivir	Decreased absorption concentration and loss of boceprivir activity	Avoid
CYP3A4/5, 2B6 inducers	Increased efavirenz metabolism reduces efavirenz effectiveness	Monitor and consider dose increases of efavirenz
CYP3A4/5, 2B6 inhibitors	Decreased efavirenz metabolism increases risk of efavirenz toxicity	Monitor and consider dose decreases of efavirenz
CYP2C9, 2C19 substrates	Decreased metabolism and increased toxicity substrates	Avoid sensitive substrates or increase monitoring and consider dose adjustments
CYP3A4/5, 2B6 substrates	Increased metabolism and decreased efficacy of substrates	Avoid sensitive substrates or increase monitoring and consider dose adjustments
Cisapride	Additive risk of arrhythmias	Contraindicated
Oral contraceptives	Reduced efficacy of oral contraceptives, unknown mechanism	Use an alternative form of contraception

Adverse Reactions: Efavirenz

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Anxiety, insomnia, headaches, rash, nausea, vomiting, diarrhea, hyperlipidemia	Fatigue, pruritus, hyperglycemia, elevated LFTs, neutropenia	Psychosis, seizures, hepatic failure, hypersensitivity, pancreatitis, suicidal ideation, fat redistribution, immune reconstitution syndrome

Efficacy Monitoring Parameters. HIV viral load, CD4 count, HIV resistance testing prior to starting therapy.

Toxicity Monitoring Parameters. LFTs, bilirubin, CBCs, lipid panel.

Key Patient Counseling Points. Multiple, potentially serious drug interactions, do not take new medications, OTCs, or herbals without consulting health-care provider. Take on an empty stomach at bedtime. Do not open, chew, or crush capsule. Does not prevent transmission of HIV, practice safe sex. May cause drowsiness, avoid driving and concurrent CNS depressants.

Clinical Pearls. Not recommended for children <3 y of age. Efavirenz is the non-nucleoside reverse transcriptase inhibitor of choice for initial combination therapy for HIV.

ELETRIPTAN: Relpax

Class: Antimigraine Serotonin Receptor Agonist

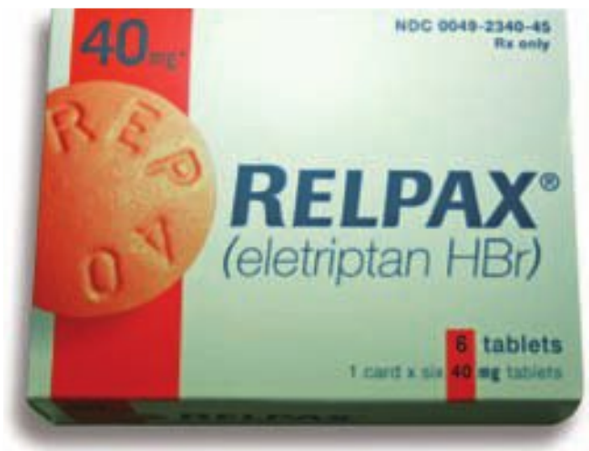
Dosage Forms. Oral Tablet: 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Migraine: 20-40 mg po at onset of migraine, may repeat after 2 h prn; *max* single dose 40 mg, *max* daily dose 80 mg/d

Off-Label Uses. None

MOA. Eletriptan binds with high affinity to serotonin (5-HT) subtypes 1B, 1D, and 1F receptors. It has no significant affinity or pharmacological activity at adrenergic α_1, α_2, or β; dopaminergic D_1 or D_2; muscarinic; or opioid receptors. Serotonin receptor agonists are believed to be effective in migraine, either through vasoconstriction (via activation of 5-HT_1 receptors located on intracranial blood vessels) or through activation of 5-HT_1 receptors on sensory nerve endings in the trigeminal system, resulting in the inhibition of pro-inflammatory neuropeptide release.



Pfizer 40 mg pictured

E

Drug Characteristics: Eletriptan

Dose Adjustment Hepatic	Avoid in severe hepatic dysfunction	**Absorption**	F = 50%, high-fat food increases bioavailability 20-30%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 138 L
Dialyzable	Unknown	**Metabolism**	Hepatic; substrate of CYP3A4/5
Pregnancy Category	C	**Elimination**	Nonrenal elimination 90% with a half-life of 4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to eletriptan, cerebrovascular syndromes, hemiplegic or basilar migraine, ischemic bowel disease, ischemic heart disease, peripheral vascular disease, severe hepatic impairment, uncontrolled hypertension	**Black Box Warnings**	None

Medication Safety Issues: Eletriptan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Sumatriptan	No

Drug Interactions: Eletriptan

Typical Agents	Mechanism	Clinical Management
SSRIs	Additive serotonergic effects	Avoid concurrent use; if not possible, monitor carefully for signs of serotonin syndrome
CYP3A4/5 inducers	Increased eletriptan metabolism reduces eletriptan effectiveness	Monitor and consider dose increases of eletriptan
CYP3A4/5 inhibitors	Decreased eletriptan metabolism increases risk of eletriptan toxicity	Monitor and consider dose decreases of eletriptan
Other 5HT agonists	Additive pharmacologic effect leading to additive toxicity	Administration within 24 h of other serotonin agonists is contraindicated

Adverse Reactions: Eletriptan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weakness	Nausea, asthenia, dizziness, somnolence	Angina, cardiac dysrhythmia, coronary arteriosclerosis, heart block, hypertension, acute myocardial infarction, aphasia, cerebral ischemia, stroke, dystonia, hemiplegia, neuropathy, transient ischemic attack, oculogyric crisis

Efficacy Monitoring Parameters. Resolution of signs of migraine headache.

Toxicity Monitoring Parameters. Seek medical attention for signs of ischemic bowel disease (eg, sudden severe abdominal pain, bloody diarrhea) or peripheral vascular disease (eg, Raynaud syndrome), serotonin syndrome (eg, agitation, hallucinations, tachycardia, hyperreflexia, incoordination, diarrhea, nausea), ischemic cardiac syndrome, or hypertensive crisis.

Key Patient Counseling Points. Should avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause dizziness or somnolence.

Clinical Pearls. These agents are not for prophylaxis—these are used for the treatment of acute migraine headache. Several serotonin agonists ("triptans") exist for migraine, administered via a variety of routes (oral, inhaled, and injected). Each differs in onset and duration of action. If 1 agent is ineffective at *max* dose, recommend changing agents or route. Instruct patient to take a second dose 2 or more h after the first, if needed, and no more than 80 mg/d.

EMTRICITABINE/TENOFOVIR: Truvada

Class: Antiretroviral Agent, Reverse Transcriptase Inhibitor; Antiretroviral Agent, Reverse Transcriptase Inhibitor

Dosage Forms. Oral Tablet: Emtricitabine/Tenofovir 200 mg/300 mg

Gilead 200 mg/300 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Treatment of HIV-1 infection in combination with other antiretroviral agents: Adults and Children ≥12 y of age, 1 tablet po daily
2. Preexposure prophylaxis (PrEP) for prevention of HIV-1 infection in adults who are at high risk for acquiring HIV: 1 tablet po daily (high risk is defined as inconsistent condom use, incarcerated, drug, and alcohol dependence)

Off-Label Uses.

1. Treatment of hepatitis B in patients with antiviral-resistant HBV or coinfection with HIV: 1 tablet po daily

MOA. Emtricitabine is a cytidine analogue while tenofovir is an analogue of adenosine 5′-monophosphate. Each drug interferes with HIV viral RNA-dependent DNA polymerase resulting in inhibition of viral replication.

Drug Characteristics: Emtricitabine/Tenofovir

Dose Adjustment Hepatic	Not required	**Absorption**	Emtricitabine F = 92%; tenofovir F = 25%, no food effect
Dose Adjustment Renal	CrCl = 30-49 mL/min, increase dose interval to 48 h; CrCl <30 mL/min, avoid	**Distribution**	Emtricitabine, saliva, semen; tenofovir, lymphocytes
Dialyzable	No	**Metabolism**	Minimal; tenofovir induces P-glycoprotein
Pregnancy Category	B	**Elimination**	Emtricitabine, half-life of 10 h; tenofovir, half-life of 17 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Resistance is associated with HIV mutations
Contraindications	Do not use for preexposure prophylaxis in patients with unknown or HIV-1 positive status. Only for use in combination with other antiretrovirals.	**Black Box Warnings**	Hepatitis B, lactic acidosis, preexposure prophylaxis

Medication Safety Issues: Emtricitabine/Tenofovir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	No	No

Drug Interactions: Eletriptan/Tenofovir

Typical Agents	Mechanism	Clinical Management
Atazanavir	Decreased atazanavir, unknown mechanism	Concurrent administration requires ritonavir boost
Didanosine	Increased bioavailability and toxicity of didanosine, unknown mechanism	Avoid
Lopinavir, ritonavir, tipranavir	Increased tenofovir bioavailability, unknown mechanism	Monitor for tenofovir toxicity; consider dose reductions
P-glycoprotein substrates	Induction of substrate metabolism decreases effectiveness of substrate	Monitor and consider substrate dose increase

Adverse Reactions: Emtricitabine/Tenofovir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hyperpigmentation, rash, hypophosphatemia, nausea, diarrhea, dizziness, insomnia, fatigue	Hyperglycemia, hyperlipidemia, anemia, neutropenia, elevated LFTs, neuropathy, hematuria	Lactic acidosis, HBV exacerbations, renal failure

Efficacy Monitoring Parameters. Prior to therapy, HIV resistance testing, HBV testing as acute, and severe exacerbations of HBV have been reported following discontinuation of antiretroviral therapy. HIV viral load, CD4 count, for assessment of efficacy. If using for preexposure prophylaxis, patients must be HIV negative. Patients receiving preexposure prophylaxis who get HIV may be drug resistant at diagnosis. Also test for sexually transmitted diseases and treat as necessary.

Toxicity Monitoring Parameters. LFTs, bilirubin, CBC, glucose, renal function, phosphorus, assessment of osteoporosis. Lactic acidosis and severe hepatomegaly and sometimes fatal steatosis have been reported with nucleoside and nucleotide analogues.

Key Patient Counseling Points. Take with or without food.

Clinical Pearls. Not recommended for children <12 y of age. Recommended as a component of preferred regimens (in combination with atazanavir/ritonavir or darunavir/ritonavir or efavirenz or raltegravir) in antiretroviral-naive patients.

ENALAPRIL: Vasotec, Various

Class: ACE-I, Antihypertensive

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg; **Oral Solution:** 1 mg/mL

Wockhardt generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: Infants ≥4 d of age, 0.1-0.5 mg/kg po daily, *max* 0.94 mg/kg po daily; Adults, 2.5 mg po daily or bid, *max* 40 mg po daily in divided doses
2. Hypertension: Infants ≥1 mo of age and Adolescents, 0.08 mg/kg up to 5 mg po daily, *max* 0.58 mg/kg or 40 mg po daily; Adults, 5 mg po daily, *max* 40 mg po daily in divided doses
3. Kidney disease, nondiabetic: Children 7-18 y of age, 0.1-0.5 mg/kg po daily, *max* 20 mg po daily; Adults, 5 mg po daily, *max* 20 mg po daily

Off-Label Uses.

1. Diabetic nephropathy: 5-20 mg po daily
2. MI: 2.5 mg po daily, may titrate to 20 mg po daily

MOA. Enalapril is a prodrug that is rapidly converted to its active metabolite, enalaprilat, a competitive ACE-I. It reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, inhibits the sympathetic nervous system, and inhibits the tissue renin–angiotensin system. The net effect is reduction in total peripheral resistance and blood pressure in hypertensive patients, and reduction of elevated afterload in patients with heart failure.

Drug Characteristics: Enalapril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%, no effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, initial dose 2.5 mg po daily, *max* 40 mg po daily	**Distribution**	50-60% protein bound
Dialyzable	Yes	**Metabolism**	Extensive hepatic to 1 active metabolite
Pregnancy Category	D	**Elimination**	Renal elimination is 61% with a half-life of 1.3 h (parent drug) and 11 h (metabolite)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to enalapril, history of angioedema, pregnancy	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Enalapril

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Elavil	No

Drug Interactions: Enalapril

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics, ARBs, potassium supplements	Increased risk of hypotension and nephrotoxicity (diuretics and ARBs), hyperkalemia	Avoid concurrent use or monitor BP, SCr, and serum potassium levels
NSAIDs, aspirin	Decreased antihypertensive effect of enalapril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr
Aliskiren	Increased risk of hyperkalemia	Concurrent use contraindicated
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use; monitor for anemia or leucopenia
Cyclosporine	Increased risk of nephrotoxicity	Avoid concurrent use or monitor SCr

Adverse Reactions: Enalapril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Increased SCr	Diarrhea, dizziness, dry cough, fatigue, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia	Angioedema, birth defects, liver failure

Efficacy Monitoring Parameters. Decreased BP, signs of heart failure.

Toxicity Monitoring Parameters. Signs of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, and urine protein.

Key Patient Counseling Points. Use potassium supplements or salt substitutes only under medical supervision.

Clinical Pearls. Progressive renal impairment including acute renal failure may occur on enalapril therapy. Injectable formulation, enalaprilat, also available. Injectable and oral dosing not interchangeable.

ENOXAPARIN: Lovenox, Various

Class: Anticoagulant

Dosage Forms. **Prefilled Syringes**: 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL; **Multiple-Dose Vial:** 300 mg/3 mL

Common FDA Label Indication, Dosing, and Titration.

1. Deep vein thrombosis prophylaxis, abdominal surgery: 40 mg sq once 2 h prior to surgery, then daily × 7-10 d
2. Deep vein thrombosis prophylaxis, hip or knee replacement surgery: 30 mg sq q12h starting 12-24 h postoperatively × 7-14 d
3. Deep vein thrombosis prophylaxis, acute medical illness: 40 mg sq daily × 6-11 d
4. Deep vein thrombosis treatment: 1 mg/kg sq q12h; initiate warfarin therapy as soon as possible and continue enoxaparin for at least 5 d and until target INR is reached
5. Acute ST segment elevation myocardial infarction: Age <75 y, 30 mg IV together with 1 mg/kg sq once, then 1 mg/kg sq q12h (*max* of 100 mg for the first 2 doses only); age ≥75 y, 0.75 mg/kg sq q12h (no initial bolus)
6. Unstable angina and non–Q-wave myocardial infarction: 1 mg/kg sq q12h × 2-8 d with aspirin 100-325 mg po daily

Off-Label Uses. None

MOA. Enoxaparin is a low-molecular-weight heparin which has antifactor Xa and IIa properties.

Drug Characteristics: Enoxaparin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100% following sq dose
Dose Adjustment Renal	CrCl <30 mL/min: avoid use or reduce dose by 50%	**Distribution**	Vd = 4.3 L
Dialyzable	Not dialyzable	**Metabolism**	Hepatic
Pregnancy Category	B	**Elimination**	Renal elimination is 40% with a half-life of 7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to enoxaparin, heparin, or pork products; active major bleeding; concurrent neuraxial analgesia	**Black Box Warnings**	Neuraxial anesthesia may cause hematomas

Sanofi-Aventis 100 mg/mL pictured

Medication Safety Issues: Enoxaparin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Lasix, Lotronex	No

Drug Interactions: Enoxaparin

Typical Agents	Mechanism	Clinical Management
NSAIDs, antiplatelet agents, thrombolytics	Increased risk of bleeding by combined effects on platelet function	Avoid or discontinue concurrent use if possible; monitor carefully for bleeding complications

Adverse Reactions: Enoxaparin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Anemia, hemorrhage	Diarrhea, nausea, thrombocytopenia, increased LFTs, fever	Atrial fibrillation, heart failure, eczematous drug eruption, intracranial hemorrhage

Efficacy Monitoring Parameters. Prevention or resolution of thrombosis, depending on indication.

Toxicity Monitoring Parameters. Signs and symptoms of bleeding, CBC, LFTs. Patients with renal failure, obese patients, pregnant patients, and others at risk of bleeding complications should be monitored using antifactor Xa testing.

Key Patient Counseling Points. If self-administered (outside health-care facility), instruct patient on appropriate administration technique. Monitor for signs of thrombosis and bleeding complications.

Clinical Pearls. Unlike unfractionated heparin, low-molecular-weight heparins cannot be monitored using standard activated partial thromboplastin time (aPTT). Antifactor Xa levels are needed for monitoring. Epidural or spinal hematomas may occur in patients who receive low-molecular-weight heparins for neuraxial anesthesia, who undergo spinal puncture, or who have an indwelling epidural catheter.

ENTECAVIR: Baraclude, Various

Class: Antiretroviral Agent, Reverse Transcriptase Inhibitor

Dosage Forms. Oral Tablet: 0.5 mg, 1 mg; **Oral Solution:** 0.05 mg/1 mL

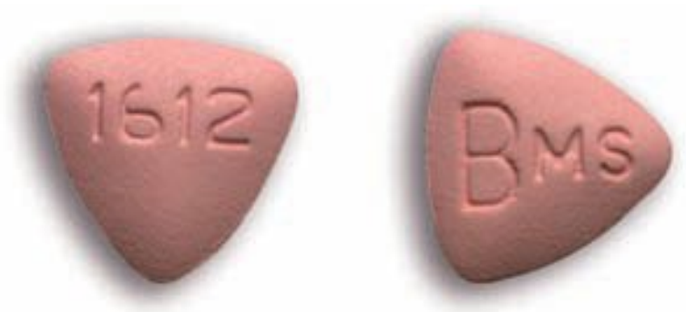
Common FDA Label Indication, Dosing, and Titration.

1. Treatment of chronic HBV infection: Adults, 0.5-1 mg po daily

Off-Label Uses.

1. HBV reinfection prophylaxis: Adults, 0.5-1 mg po daily

MOA. Intracellularly phosphorylated to guanosine triphosphate which competes with natural substrates to effectively inhibit HBV polymerase; enzyme inhibition blocks reverse transcriptase activity thereby reducing viral DNA synthesis.



Bristol-Myers Squibb 1 mg pictured

E

Drug Characteristics: Entecavir

Dose Adjustment Hepatic	Not required	**Absorption**	F approaches 100%, food decreases absorption by 50%
Dose Adjustment Renal	CrCl <50 mL/min, increase interval	**Distribution**	Extensive tissue
Dialyzable	Yes, administer after dialysis	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	60-70% renal, half-life 140 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Resistance is associated with HBV mutations
Contraindications	None	**Black Box Warnings**	HIV resistance in chronic hepatitis B patients with unrecognized or untreated HIV infection; discontinuation of therapy may result in disease exacerbation; lactic acidosis

Medication Safety Issues: Entecavir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Entecavir

Typical Agents	Mechanism	Clinical Management
Ribavirin	Increased hepatotoxicity	Avoid concurrent use
Ganciclovir	Increased hematologic toxicity	Avoid concurrent use

Adverse Reactions: Entecavir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, elevated LFTs	Nausea, vomiting, diarrhea, headaches, hematuria, hyperglycemia, hepatic encephalopathy	Hypersensitivity, renal failure, hepatomegaly, and thrombocytopenia

Efficacy Monitoring Parameters. HBV DNA, LFTs.

Toxicity Monitoring Parameters. HIV status (prior to initiation of therapy); LFTs, renal function. Call health-care provider for dark urine or yellow skin or eyes.

Key Patient Counseling Points. Complete full course of therapy; take on an empty stomach.

Clinical Pearls. Hepatitis may get worse if this drug is stopped; monitor HBV DNA after discontinuation. Consider genetic testing of HBV if suboptimal response to therapy.

EPINEPHRINE: EpiPen, EpiPen Jr., Various

Class: Anaphylaxis Agent

Dosage Forms. Auto-Injector Kit: Delivers 0.3 mg epinephrine in 0.3 mL (1:1000 solution) or 0.15 mg epinephrine in 0.3 mL (1:2000 solution)

Common FDA Label Indication, Dosing, and Titration.

1. Emergency treatment of acute anaphylaxis due to allergic reactions: Children 15-30 kg, 0.15 mg (0.3 mL of a 1:2000 solution) IM or sq; Children >30 kg and Adults, 0.3 mg (0.3 mL of a 1:1000 solution) IM or sq; may be repeated if severe anaphylaxis persists

Off-Label Uses. None

MOA. Epinephrine treats severe allergic reactions to insect stings or bites, foods, drugs, and other allergens. It acts on both α- and β-adrenergic receptors. Through its action on α-adrenergic receptors, epinephrine lessens the vasodilation and increased vascular permeability that occurs during anaphylaxis, which can lead to loss of intravascular fluid volume and hypotension. Through its action on β-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation that helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis. Epinephrine also alleviates pruritus, urticaria, and angioedema.

Dey 0.3 mg pictured

Drug Characteristics: Epinephrine

Dose Adjustment Hepatic	Not required	**Absorption**	20% of dose rapidly absorbed after sq dose; remaining 80% absorbed over 6-8 h
Dose Adjustment Renal	Not required	**Distribution**	N/A
Dialyzable	Not dialyzable	**Metabolism**	Rapid and complete hepatic
Pregnancy Category	C	**Elimination**	Inactivated metabolites renally
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	None in emergency situations	**Black Box Warnings**	None

Medication Safety Issues: Epinephrine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Jr.	EPINEPHrine	No	Yes	Epifrin, ePHEDrine	No

Drug Interactions: Epinephrine

Typical Agents	Mechanism	Clinical Management
Cardiac glycosides	Combination may result in cardiac arrhythmias	Monitor closely for signs of arrhythmia
Beta-blockers, alpha-blockers	Effects of epinephrine are antagonized	Monitor closely for lack of response to epinephrine
TCAs, MAOIs, levothyroxine, linezolid	The effects of epinephrine may be potentiated due to inhibition of norepinephrine reuptake	Monitor closely for hypertension, cardiac arrhythmias

Adverse Reactions: Epinephrine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Palpitations, pale complexion, sweating, nausea, vomiting, asthenia, dizziness, headache, tremor, anxiety, apprehension, restlessness		Angina, autonomic hyperreflexia, cardiac dysrhythmia, ventricular fibrillation, pulmonary edema

Efficacy Monitoring Parameters. Resolution of symptoms of anaphylaxis (dyspnea, pruritus, urticaria, angioedema).

Toxicity Monitoring Parameters. Seek medical attention after emergency use and monitor for signs of cardiac toxicity and hypertension.

Key Patient Counseling Points. Instruct patient on proper administration technique. Immediately seek medical assistance, even if the patient feels better after epinephrine use.

Clinical Pearls. Epinephrine auto-injectors are intended for immediate self-administration as emergency supportive therapy only and are not a substitute for immediate medical care. Epinephrine is used for a wide variety of indications in the acute care setting, including in cardiac resuscitation attempts, and in combination with topical anesthetic as a vasodilator to reduce bleeding during suturing and other minor surgical procedures. Ophthalmic and inhaled dosage forms also available for other indications.

EPOETIN: Epogen, Procrit

Class: Erythropoietic Stimulating Agent

Dosage Forms. **Injection Solution:** 2000 units/mL, 3000 units /mL, 4000 units/mL, 10,000 units/mL, 20,000 units/mL

Common FDA Label Indication, Dosing, and Titration.

1. Anemia of cancer chemotherapy: Children, 600 units/kg (*max* 40,000 units) IV once weekly; Adults, 40,000 units sq weekly; dose adjusted based on changes in Hgb levels
2. Anemia of chronic renal failure: Children, 50 units/kg IV or sq 3 times per week; Adults not on dialysis, 10,000 units sq weekly, 20,000 units sq every other week, 30,000 units every 3rd wk, or 40,000 units sq every 4 wk; Adults on dialysis, 50-100 units/kg IV or sq 3 times per week; dose adjusted based on changes in Hgb levels
3. Perioperative collection of blood for allogeneic infusion: 300 units/kg/d sq for 10 d before surgery, on the day of surgery, and for 4 d postoperatively

Off-Label Uses.

1. Anemia due to myelodysplastic syndrome: 40,000-60,000 units sq 1-3 times/wk

MOA. Epoetin alfa is recombinant human erythropoietin. It binds to the erythropoietin receptor on erythroid progenitor cells, stimulating production/differentiation of mature red cells.

Amgen 4000 units/mL pictured

E

Drug Characteristics: Epoetin

Dose Adjustment Hepatic	Not required	**Absorption**	Subcutaneously, F = 22-33%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 52 mL/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatic via galactose receptors
Pregnancy Category	C	**Elimination**	Renal elimination is minimal with a half-life of 4-13 h IV for CKD pts, and 16-67 h for anemic cancer pts
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to epoetin, albumin, uncontrolled hypertension	**Black Box Warnings**	Increased CV, stroke, mortality risk; cancer recurrence; REMS program

Medication Safety Issues: Epoetin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Neupogen, darbepoetin	No

Drug Interactions: Epoetin

Typical Agents	Mechanism	Clinical Management
Thalidomide	Additive risk of thrombosis	Avoid concurrent use if possible; consider anticoagulation if agents must be combined

Adverse Reactions: Epoetin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, hypertension, diarrhea, injection site thrombosis, myalgia, fatigue	Thromboembolism, myocardial infarction	Pure red cell aplasia, immune hypersensitivity, seizures, tumor progression

Efficacy Monitoring Parameters. Monitor Hgb carefully and titrate dose to avoid transfusion and reduce or interrupt therapy if Hgb approaches 11 g/dL. Iron studies needed to ensure adequate iron stores, transferrin saturation >20% and ferritin >100 ng/mL.

Toxicity Monitoring Parameters. BP, weight to monitor edema, SCr in renal failure patients.

Key Patient Counseling Points. Do not shake, dilute, or expose to light. Store in box in refrigerator. Do not combine remainders from different vials; each vial is single use. May require several weeks for maximum effect.

Clinical Pearls. Typically administered in hospitals and clinics only. In cancer patients with certain tumor types (eg, breast, non–small cell lung, head and neck, lymphoid, cervical), epoetin and darbepoetin shortened overall survival and/or increased the risk of tumor progression or recurrence in some clinical studies. Discontinue after the completion of the chemotherapy course and if no response after 8 wk of therapy. Hospitals and health-care professionals who prescribe and/or dispense epoetin to patients with cancer must enroll and comply with the ESA APPRISE oncology program at www.esa-apprise.com. Renal failure patients experienced greater risks of death, stroke, and serious cardiovascular events when administered erythropoiesis-stimulating agent to target Hgb levels of 13 g/dL or higher in clinical studies. Clinical trials have shown that epoetin provides no improvement in quality of life, fatigue, or well-being.

ESCITALOPRAM: Lexapro, Various

Forest Laboratories pictured

Class: SSRI Antidepressant

Dosage Forms. Oral Tablet: 5 mg, 10 mg, 20 mg; **Oral Solution:** 5 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Children ≥ 12 y of age and Adults, 10 mg po daily, may titrate to 20 mg po daily
2. Generalized anxiety disorder: 10 mg po daily, may titrate to 20 mg po daily

Off-Label Uses.

1. OCD: 20-60 mg po daily
2. Panic disorder: 20-30 mg po daily, may titrate to 60 mg po daily
3. Hot flashes: 10 mg once po daily, may increase to 20 mg once daily after 4 wk

MOA. Escitalopram is the s-enantiomer of racemic citalopram and is an antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI). It does not affect reuptake of norepinephrine or dopamine and has a relative lack of affinity for muscarinic, histamine, α_1- and α_2-adrenergic, and serotonin receptors.

Drug Characteristics: Escitalopram

Dose Adjustment Hepatic	Dose at 10 mg po daily	**Absorption**	F = 80%, food has no effect on absorption
Dose Adjustment Renal	Use with caution in severe renal impairment	**Distribution**	Vd = 12 L/kg; 56% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5, CYP2C19
Pregnancy Category	C	**Elimination**	Renal elimination is 10% with a half-life of 22-32 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to citalopram or escitalopram; concurrent MAOI use	**Black Box Warnings**	Suicidality; not approved for use in children

Medication Safety Issues: Escitalopram

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Loxitane	No

Drug Interactions: Escitalopram

Typical Agents	Mechanism	Clinical Management
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Triptans	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination)
Linezolid, MAOIs	Increased risk of serotonin syndrome	Concomitant use contraindicated
Lithium	Increased lithium concentrations	Monitor for lithium side effects and consider dose decreases
CYP3A4/5, 2C19 inducers	Increased escitalopram metabolism reduces escitalopram effectiveness	Monitor and consider dose increases of escitalopram
CYP3A4/5, 2C19 inhibitors	Decreased escitalopram metabolism increases risk of escitalopram toxicity	Monitor and consider dose decreases of escitalopram

Adverse Reactions: Escitalopram

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, nausea, sedation	Constipation, diaphoresis, diarrhea, disorder of ejaculation, dizziness, fatigue, impotence, indigestion, insomnia, rash, reduced libido, somnolence, vomiting, weight gain, xerostomia	Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsades de pointes

Efficacy Monitoring Parameters. Improvement in symptoms of depression, panic disorder (dyspnea, palpitations, trembling, experiencing an uncontrolled feeling, etc); OCD (recurrent and persistent impulses that are intrusive and senseless, or repetitive and intentional behaviors performed in response to obsessive thoughts); or generalized anxiety.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for 4-6 wk. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

Clinical Pearls. If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate.

ESOMEPRAZOLE: Nexium, Various

Class: Proton Pump Inhibitor

Dosage Forms. **Oral Capsule, Delayed Release:** 20 mg, 40 mg; **Oral Granules:** 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. *H. pylori* GI infection: 40 mg po daily × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
2. Erosive esophagitis, GERD treatment: Children 1-11 y of age and <20 kg, 10 mg po daily × 8 wk; Children ≥20 kg, 10-20 mg po daily × 8 wk; Adults, 20-40 mg po daily × 4-8 wk
3. Erosive esophagitis, heartburn: Children 1-11 y of age, 10 mg po daily × 8 wk; Children ≥12 y of age and Adults, 20-40 mg po daily × up to 8 wk
4. Prevention of NSAID-induced gastropathy: 20-40 mg po daily × up to 6 mo
5. Zollinger-Ellison syndrome: 40 mg po bid up to 240 mg/d

AstraZeneca pictured

Off-Label Uses. None

MOA. Esomeprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^+/K^+-ATPase (proton pump), which is the final pathway for acid secretion. Esomeprazole produces a profound and prolonged antisecretory effect, and inhibits basal, nocturnal, pentagastrin-stimulated, and food-stimulated gastric acid secretion.

Drug Characteristics: Esomeprazole

Dose Adjustment Hepatic	Severe, *max* dose of 20 mg daily	**Absorption**	F = 90%, food reduces F by 50%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 16 L; 97% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP2C19; inducer of CYP2C19
Pregnancy Category	B	**Elimination**	Renal elimination is 80% with a half-life of 60-90 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	3% of Caucasians are poor CYP2C19 metabolizers; if known, consider 20 mg dose; moderate CYP2C19 inhibitor
Contraindications	Hypersensitivity to omeprazole or esomeprazole	**Black Box Warnings**	None

Medication Safety Issues: Esomeprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	NexIUM	Capsules	No	NexAVAR	No

Drug Interactions: Esomeprazole

Typical Agents	Mechanism	Clinical Management
Clopidogrel	Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness	Avoid concurrent use
CYP2C19 inhibitors	Decreased esomeprazole metabolism increases risk of esomeprazole toxicity	Consider dose decreases of esomeprazole
CYP2C19 inducers	Increased esomeprazole metabolism reduces esomeprazole effectiveness	Consider dose increases of esomeprazole
CYP2C19 substrates	Decreased metabolism and increased toxicity of substrates	Avoid concurrent use or decrease substrate dose
pH-dependent drugs	Lower gastric pH reduces absorption	Monitor for lack of effectiveness of interacting drug and adjust dose as necessary
Warfarin	Increased anticoagulant effect	Monitor INR and adjust warfarin dose accordingly

Adverse Reactions: Esomeprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Abdominal pain, diarrhea, nausea, flatulence	Toxic epidermal necrolysis, pancreatitis, hepatotoxicity, bone fracture, rhabdomyolysis, acute interstitial nephritis

Efficacy Monitoring Parameters. Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

Toxicity Monitoring Parameters. Severe headache or blistering skin rash.

Key Patient Counseling Points. Should be taken 1 h before meals.

Clinical Pearls. Multiple *H. pylori* regimens contain different combinations of PPIs and antibiotics; complete full regimen if prescribed for *H. pylori* treatment. Many PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently. Also available in injectable formulation. Increased risk of fractures; use lowest effective dose in patients at risk for osteoporosis. Reassess for continuation after treatment duration is complete.

ESTRADIOL ORAL: Estrace, Various

Class: Estrogen

Dosage Forms. Oral Tablet: 0.5 mg, 1 mg, 2 mg

Barr generic 1 mg pictured

Watson generic 0.5 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Abnormal vasomotor function (moderate to severe), menopause: 1-2 mg po daily for 21 d followed by 7 d off
2. Atrophic vulva or vagina (moderate-severe), menopause: Oral tablet, 1-2 mg po daily in a cyclical pattern (3 wk on, 1 wk off)
3. Breast cancer, metastatic, for palliation only: 10 mg po tid × 3 mo
4. Carcinoma of prostate, advanced, androgen-dependent, for palliation only: 1-2 mg po tid
5. Decreased estrogen level, secondary to hypogonadism, castration, or primary ovarian failure: 1-2 mg po daily
6. Postmenopausal osteoporosis, prophylaxis: 0.5 mg po daily for 23 d followed by 5 d off

Off-Label Uses. None

MOA. Estradiol (17β-estradiol; E2) is the most potent of the naturally occurring estrogens and the major estrogen secreted during the reproductive years. Estradiol and other estrogens produce characteristic effects on specific tissues (such as breast), cause proliferation of vaginal and uterine mucosa, increase calcium deposition in bone, and accelerate epiphyseal closure after initial growth stimulation.

Drug Characteristics: Estradiol Oral

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Widely distributed; 98% protein bound
Dialyzable	Yes	**Metabolism**	Extensive hepatic; substrate of many CYP pathways, major substrate of CYP3A4/5, 1A2, P-glycoprotein
Pregnancy Category	X	**Elimination**	Renal with a half-life of 21 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to estradiol; history of thromboembolic disorders, breast cancer, any estrogen-dependent neoplasm, known or suspected pregnancy	**Black Box Warnings**	Endometrial and breast cancer risk, dementia risk; should not be used to reduce CV risk

Medication Safety Issues: Estradiol Oral

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Aldara	Avoid oral and topical patch

Drug Interactions: Estradiol Oral

Typical Agents	Mechanism	Clinical Management
CYP3A4/5, 1A2, P-glycoprotein inducers	Increased estradiol metabolism reduces estradiol effectiveness	Consider dose increases of estradiol
CYP3A4/5, 1A2 , P-glycoprotein inhibitors	Decreased estradiol metabolism increases risk of estradiol toxicity	Consider dose decreases of estradiol

Adverse Reactions: Estradiol Oral

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Weight change, nausea, vomiting, disturbance in mood, swelling of breast, depression	Heart disease, MI, DM, venous thromboembolism, anaphylaxis, cerebrovascular accident, pulmonary embolism, breast, endometrial or ovarian cancer

Efficacy Monitoring Parameters. Improvement in menopause symptoms; improved BMD for postmenopausal osteoporosis.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam.

Key Patient Counseling Points. Report abnormal vaginal bleeding or signs/symptoms of a thromboembolic disorder. Do not smoke during therapy, as this increases the risk of thromboembolic events.

Clinical Pearls. Estrogens increase the risk of endometrial cancer; monitor for abnormal vaginal bleeding. Increased risks of MI, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women have been reported. An increased risk of developing dementia in women ≥65 y of age has also been reported. Estrogens, with or without progestins, should be prescribed at the lowest effective doses and for the shortest duration possible. Also available in a variety of topical and vaginal formulations.

ESTRADIOL TRANSDERMAL PATCH: Vivelle-DOT, Estraderm, Various

Class: Estrogen

Dosage Forms. **Transdermal Patch:** 0.025 mg/d, 0.0375 mg/d, 0.05 mg/d, 0.075 mg/d, 0.1 mg/d

Common FDA Label Indication, Dosing, and Titration.

1. Abnormal vasomotor function or atrophic vagina or vulva (moderate-severe), menopause: 0.0375 mg/d patch applied to the skin twice weekly
2. Postmenopausal osteoporosis, prophylaxis: 0.025 mg/d patch applied to the skin twice weekly

Off-Label Uses. None

MOA. Estradiol (17β-estradiol; E2) is the most potent of the naturally occurring estrogens and the major estrogen secreted during the reproductive years. Estradiol and other estrogens produce characteristic effects on specific tissues (such as breast), cause proliferation of vaginal and uterine mucosa, increase calcium deposition in bone, and accelerate epiphyseal closure after initial growth stimulation.

Novartis 0.05 mg/day pictured

Drug Characteristics: Estradiol Transdermal Patch

Dose Adjustment Hepatic	Not required	**Absorption**	F improved by bypassing first-pass metabolism
Dose Adjustment Renal	Not required	**Distribution**	Widely distributed; 98% protein bound
Dialyzable	Yes	**Metabolism**	Extensive hepatic; substrate of many CYP pathways, major substrate of CYP3A4/5, 1A2, P-glycoprotein
Pregnancy Category	X	**Elimination**	Renal with a half-life of 21 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to estradiol; history of thromboembolic disorders, breast cancer, any estrogen-dependent neoplasm, pregnancy	**Black Box Warnings**	Endometrial and breast cancer risk, dementia risk; should not be used to reduce CV risk

Medication Safety Issues: Estradiol Transdermal Patch

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Aldara	Avoid oral and topical patch

Drug Interactions: Estradiol Transdermal Patch

Typical Agents	Mechanism	Clinical Management
CYP3A4/5, 1A2, P-glycoprotein inducers	Increased estradiol metabolism reduces estradiol effectiveness	Consider dose increases of estradiol
CYP3A4/5, 1A2 , P-glycoprotein inhibitors	Decreased estradiol metabolism increases risk of estradiol toxicity	Consider dose decreases of estradiol

Adverse Reactions: Estradiol Transdermal Patch

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, application site irritation	Weight change, nausea, vomiting, disturbance in mood, swelling of breast, depression	Heart disease, MI, DM, venous thromboembolism, anaphylaxis, cerebrovascular accident, pulmonary embolism, breast, endometrial or ovarian cancer

Efficacy Monitoring Parameters. Improvement in menopause symptoms; improved BMD evaluation for postmenopausal osteoporosis.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam.

Key Patient Counseling Points. Report abnormal vaginal bleeding or signs/symptoms of a thromboembolic disorder. Do not smoke during therapy, as this increases the risk of thromboembolic events. Place patch on clean, dry skin, preferably on the lower abdomen, upper quadrant of the buttock, or outer aspect of the hip; do not apply to the breasts or waistline; rotate sites of application with 1 wk allowed between applications to a particular site.

Clinical Pearls. Estrogens increase the risk of endometrial cancer; monitor for abnormal vaginal bleeding. Increased risks of MI, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women have been reported. An increased risk of developing dementia in women ≥65 y of age has also been reported. Estrogens, with or without progestins, should be prescribed at the lowest effective doses and for the shortest duration possible. Also available in oral and vaginal formulations. Patch contains metal, remove prior to MRI. Do not cut patch.

ESZOPICLONE: Lunesta, Various

Sunovian Pharmaceutical pictured

Class: Nonbarbiturate Hypnotic. C-IV

Dosage Forms. Oral Tablet: 1 mg, 2 mg, 3 mg

Common FDA Label Indication, Dosing, and Titration.

1. Insomnia: 2 mg po immediately before bedtime; dosing may be initiated at or titrated to 3 mg

Off-Label Uses. None

MOA. The exact mechanism of action of eszopiclone, a non-benzodiazepine hypnotic, is unknown. It is believed that eszopiclone binds to or interacts allosterically at the GABA-receptor complex domain.

Drug Characteristics: Eszopiclone

Dose Adjustment Hepatic	Severe impairment, 1 mg po qhs, *max* 2 mg/d	**Absorption**	F = 75%, high-fat meal delays absorption
Dose Adjustment Renal	Not required	**Distribution**	52-59% protein bound
Dialyzable	Unknown	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 75% with a half-life of 5-6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to eszopiclone	**Black Box Warnings**	None

Medication Safety Issues: Eszopiclone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Neulasta	Avoid chronic use (>90 d)

Drug Interactions: Eszopiclone

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased eszopiclone metabolism reduces eszopiclone effectiveness	May require 3 mg dose
CYP3A4/5 inhibitors	Decreased eszopiclone metabolism increases risk of eszopiclone toxicity	Initial dose 1 mg, monitor for side effects
Opioids, benzodiazepines	Increased CNS or respiratory depression	Avoid concomitant use

Adverse Reactions: Eszopiclone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Abnormal behavior or thinking, confusion, diarrhea, dizziness, nausea, rash, somnolence, taste disorder, vomiting, xerostomia	Anaphylaxis, angioedema

Efficacy Monitoring Parameters. Improvement in sleep onset, duration, and quality.

Toxicity Monitoring Parameters. Excessive sedation, impaired coordination.

Key Patient Counseling Points. Instruct patient to take immediately before bedtime and to not take with heavy/high-fat meal. Severe anaphylactic/anaphylactoid reactions, some fatal, have been reported. Warn patient of the risk of "sleep-driving" and other complex behaviors (eg, preparing and eating food, making phone calls) when the patient is not fully awake. Risk is increased when drug is combined with alcohol or other CNS depressants. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Patient should report insomnia that worsens or persists longer than 7-10 d. Advise patient to report abnormal thoughts or behavior (confusion, agitation, hallucinations, suicidal thoughts, new or worsening depression), memory loss, or anxiety. Instruct patient to take drug only when experiencing insomnia. This drug should not be taken on a regular schedule when insomnia is not present. Patient should not drink alcohol while taking this drug.

Clinical Pearls. Safety and efficacy not established in children. Elderly may be more susceptible; use a lower starting dose. Medication guide must be provided at dispensing.

ETHINYL ESTRADIOL AND ETONOGESTREL RING: NuvaRing

Class: Contraceptive

Dosage Forms. Vaginal Ring: Releases ethinyl estradiol 15 mcg/d and etonogestrel 0.12 mg/d

Common FDA Label Indication, Dosing, and Titration.

1. Contraception: 1 ring inserted vaginally by patient and remaining continuously for 3 wk, then removed for 1 wk; a new ring is then inserted, regardless whether bleeding has or has not finished

Off-Label Uses.

1. Treatment of menorrhagia (dose same as for contraception)
2. Dysfunctional uterine bleeding (dose same as for contraception)

MOA. See Preface C Card: General Content Related to All Oral Contraceptives

Drug Characteristics: Ethinyl Estradiol and Etonogestrel Ring

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40% for ethinyl estradiol; F = 100% for etonogestrel
Dose Adjustment Renal	Not required	**Distribution**	Vd = 45 L/kg for ethinyl estradiol; Vd = 201-245 L for etonogestrel; highly protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic via CYP3A4/5 for both components
Pregnancy Category	X	**Elimination**	Renal elimination with a half-life of 24 h for ethinyl estradiol and 23-28 h for etonogestrel
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, pregnancy; smoking 15 or more cigarettes per day	**Black Box Warnings**	Smoking risk

Schering-Plough pictured

E

Drug Interactions and Adverse Reactions: Ethinyl Estradiol and Etonogestrel Ring. See Preface C Card: **General Content Related to All Oral Contraceptives.**

Efficacy Monitoring Parameters. Lack of pregnancy.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam (in addition to monthly self-exam).

Key Patient Counseling Points. See Preface C Card: **General Content Related to All Oral Contraceptives** for drug-related counseling points. If the vaginal ring is inadvertently expelled or removed, it may be rinsed in cool to lukewarm water and reinserted as soon as possible, at the latest within 3 h. If the ring-free interval has been extended beyond 7 d or if the vaginal ring has been left in place for more than 4 wk, an additional form of contraception must be used until the vaginal ring has been used continuously for 7 d.

Clinical Pearls. Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects.

EXENATIDE: Byetta, Bydureon

Class: Glucagon-Like Peptide-1 Receptor Agonist

Dosage Forms. Subcutaneous Solution for Injection: 5 mcg/0.02 mL, 10 mcg/0.04 mL; **Subcutaneous Suspension for Injection:** 2 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, Type 2: Immediate release, 5-10 mcg sq bid; Extended release, 2 mg sq weekly

Off-Label Uses. None

MOA. Exenatide is an incretin mimetic agent that mimics the enhancement of glucose-dependent insulin secretion and several other antihyperglycemic actions of incretins. Incretins enhance glucose-dependent insulin secretion and exhibit other antihyperglycemic actions following release into circulation from the gut.

Lilly pictured

E

Drug Characteristics: Exenatide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 65-76% after sq dose
Dose Adjustment Renal	CrCl 30-50 mL/min, dose 5 mcg and increase with caution; avoid if CrCl <30 mL/min	**Distribution**	Vd = 28.3 L after sq dose
Dialyzable	Unknown	**Metabolism**	Minimal
Pregnancy Category	C	**Elimination**	Renal elimination with a half-life of 2.4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to exenatide	**Black Box Warnings**	Thyroid C-cell tumors (Bydureon)

Medication Safety Issues: Exenatide

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Exenatide

Typical Agents	Mechanism	Clinical Management
Warfarin	Increased risk of bleeding	Monitor INR and consider warfarin dose adjustments

Adverse Reactions: Exenatide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypoglycemia, diarrhea, nausea	Diaphoresis, decreased appetite, GERD, antibody development, headache, asthenia	Pancreatitis, anaphylaxis, acute renal failure, worsening of preexisting renal disease

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL; HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness; seek medical attention if severe GI upset, changes in urination, shortness of breath, or severe skin rash.

Key Patient Counseling Points. Immediate-release product is dispensed in a prefilled pen containing 60 doses. Use this medicine 1 h before eating. Store new, unused pens in the refrigerator in the original carton. After using the pen for the first time, store it in a closed container at room temperature. Remove the needle from the pen before storing the medicine. Throw the pen away after using it for 30 d, even if there is some medicine left in it. Monitor FPG in frequent intervals (2-4 times per day). Carry candy or some type of sugar with you at all times, especially if you are away from home, for episodes of hypoglycemia. Extended-release product is dispensed as powder with diluent in prefilled syringe. Patient instructions on weekly dose preparation and administration must be provided.

Clinical Pearls. Metformin is first-line therapy for type 2 diabetes. Exenatide may be added if HbA_{1c} goals are not achieved with metformin alone. Many clinicians may try an oral sulfonylurea prior to exenatide. Dose- and duration-dependent thyroid C-cell tumors have developed in animal studies with Bydureon therapy; relevance in humans unknown. May increase risk of pancreatic duct metaplasia. Medication guide required with dispensing.

EZETIMIBE: Zetia

Class: Antihyperlipidemic, Cholesterol Absorption Inhibitor

Dosage Forms. **Oral Tablet:** 10 mg

Merck 10 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Familial hypercholesterolemia-homozygous: with atorvastatin or simvastatin: Adults and Children >10 y of age, 10 mg po daily
2. Mixed hyperlipidemia: 10 mg po daily in combination with fenofibrate
3. Primary hypercholesterolemia: 10 mg po daily, alone or in combination with an HMG-CoA reductase inhibitor (statin)

Off-Label Uses. None

MOA. Ezetimibe localizes at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood; this distinct mechanism is complementary to that of statins and of fenofibrate.

E

Dose Adjustment Hepatic	Avoid if moderate or severe hepatic dysfunction	**Absorption**	F variable, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 105 L; 90% protein bound
Dialyzable	Unknown	**Metabolism**	In intestine and liver, not via CYP450
Pregnancy Category	C	**Elimination**	Renal elimination is 11% with a half-life of 9-30 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ezetimibe, gallbladder disease, severe hepatic dysfunction, concurrent use with a statin in a pregnant or nursing mother	**Black Box Warnings**	None

Medication Safety Issues: Ezetimibe

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zestril	No

Drug Interactions: Ezetimibe

Typical Agents	Mechanism	Clinical Management
Cholestyramine, colestipol	Decreased absorption of ezetimibe	Separate administration by 2-4 h
Fibrates	Increased risk of cholelithiasis	Avoid concurrent use or monitor for cholelithiasis
Warfarin	Increased risk of bleeding	Monitor INR and consider dose adjustments

Adverse Reactions: Ezetimibe

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea	Rhabdomyolysis, cholelithiasis, hepatotoxicity, agranulocytosis, pancreatitis

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain, LFT and CBC, SCr.

Key Patient Counseling Points. Take with or without food and may be taken at the same time as a concurrent statin. In patients receiving a bile acid sequestrant concurrently, ezetimibe should be taken at least 2 h before or 4 h after the bile acid sequestrant is taken.

Clinical Pearls. Statins are the most effective lipid-altering agents for decreasing LDL cholesterol, and are considered drugs of choice. Ezetimibe has modest single agent activity and is used in combination with statin or in combination with fenofibrate. Ezetimibe is also available in fixed-dose combination with simvastatin.

FAMOTIDINE: Pepcid, Various

Class: Histamine H_2 Antagonist

Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg; **Powder for Oral Suspension:** 40 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Duodenal ulcer, acute: Children >1 y, 0.5 mg/kg/d po hs, *max* of 40 mg/d; Adults, 20 mg po bid or 40 mg po daily hs
2. Duodenal ulcer, maintenance: Adults, 20 mg po daily hs
3. Gastroesophageal reflux disease: Children >1 y, 1 mg/kg/d po hs, *max* of 80 mg/d, duration based on response; Adults, 20-40 mg po bid × up to 12 wk
4. Gastric ulcer, acute: Children >1 y, 0.5 mg/kg/d po hs, *max* of 40 mg/d; Adults, 40 mg po daily hs
5. Indigestion (OTC): 10-20 mg po bid

Northstar Rx generic
20 mg pictured

Off-Label Uses. None

MOA. Famotidine is a competitive inhibitor of histamine H_2 receptors. The primary clinically important pharmacologic activity of famotidine is inhibition of gastric secretion. Both the acid concentration and the volume of gastric secretion are suppressed by famotidine, while changes in pepsin secretion are proportional to volume output.

Drug Characteristics: Famotidine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40-45%, no effect of food on absorption
Dose Adjustment Renal	Adults, CrCl <50 mL/min, reduce dose 50% or increase dosing interval to 36-48 h; children, CrCl 30-60 mL/min/1.73 m^2, administer 50% of dose; children, CrCl <30 mL/min/1.73 m^2, administer 25% of dose	**Distribution**	Vd = 1.3 L/kg; 10-20% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal
Pregnancy Category	B	**Elimination**	Renal elimination is 60% with a half-life of 2.5-3.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to famotidine or other H_2 antagonists	**Black Box Warnings**	None

Medication Safety Issues: Famotidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Max Strength	No	No	No	FLUoxetine	No

Drug Interactions: Famotidine

Typical Agents	Mechanism	Clinical Management
Cefpodoxime	Decreased cefpodoxime absorption due to increase in gastric pH caused by H_2 antagonist	Choose alternative antibiotic
pH-dependent drugs	Lower gastric pH reduces absorption	Monitor pH-dependent drug and adjust dose as necessary

Adverse Reactions: Famotidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, diarrhea, nausea, skin rash		Stevens-Johnson syndrome, increased liver enzymes, seizure

Efficacy Monitoring Parameters. Resolution of GI discomfort, resolution of ulcers shown on endoscopy.

Toxicity Monitoring Parameters. Severe blistering skin rash.

Key Patient Counseling Points. Take at bedtime. May take with food or antacids, if needed. Shake suspension well before use.

Clinical Pearls. Other PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Injectable dosage form also available; when the intravenous route is used, treatment should be converted to oral route as soon as possible to avoid cost and risks associated with intravenous therapy.

FEBUXOSTAT: Uloric

Class: Xanthine Oxidase Inhibitor

Dosage Forms. Oral Tablet: 40 mg, 80 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hyperuricemia: 40 mg po daily, may titrate to 120 mg po daily

Off-Label Uses. None

MOA. Selectively inhibits xanthine oxidase, the enzyme responsible for converting xanthine to uric acid. Lowers uric acid and reduces gout

Drug Characteristics: Febuxostat

Dose Adjustment Hepatic	Use with caution if severe hepatic dysfunction	**Absorption**	F ≥49%
Dose Adjustment Renal	Use with caution if severe renal dysfunction	**Distribution**	99% protein bound, Vd = 50L
Dialyzable	Unknown	**Metabolism**	Extensively metabolized by numerous enzymes, individual enzymes have little contribution to total metabolism
Pregnancy Category	C	**Elimination**	50% renal elimination with a half-life of 5-8 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Concurrent azathioprine or mercaptopurine	**Black Box Warnings**	None

Medication Safety Issues: Febuxostat

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Febuxostat

Typical Agents	Mechanism	Clinical Management
Substrates for xanthine oxidase (azathioprine, didanosine, mercaptopurine, theophylline)	Decreased metabolism of xanthine oxidase substrates and increased toxicity	Concurrent use of azathioprine and mercaptopurine is contraindicated; use other substrates with caution

Adverse Reactions: Febuxostat

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Rash, nausea, elevated LFTs, arthralgia	ECG abnormalities, hypersensitivity, stroke, mood changes

Efficacy Monitoring Parameters. Reduction in uric acid levels to <6 mg/dL, decrease in gout attacks.

Toxicity Monitoring Parameters. Baseline and periodic LFTs.

Key Patient Counseling Points. Take without food. Weight loss and limiting alcohol consumption will reduce gout attacks and should be recommended to all patients. Seek medical attention for severe mood swings, rashes, or abnormal heartbeat.

Clinical Pearls. When compared to allopurinol 300 mg, febuxostat is more effective in lowering uric acid levels to <6 mg/dL; however, the drugs were equivalent in terms of preventing gout flares and patients receiving feboxostat were more likely to have elevated LFTs. Allopurinol remains the mainstay for prevention of gout flares and febuxostat is an alternative for patients unable to tolerate or without a satisfactory response to allopurinol. An increase in gout flares is typically seen when initiating agents such as febuxostat. Prophylactic therapy with NSAIDs at initiation of therapy for up to 6 mo may be beneficial to prevent gout flares.

FELODIPINE: Plendil, Various

Class: Calcium Channel Blocker

Dosage Forms. Oral Tablet, Extended Release: 2.5 mg, 5 mg, 10 mg

Common FDA Label Indication and Dosing.

1. Hypertension: Children, 0.1-0.6 mg/kg/d po; Adults, 2.5-10 mg po daily

Off-Label Uses. None

MOA. Felodipine is a dihydropyridine calcium-channel-blocking drug with potent arterial and coronary vasodilating properties. A reflex increase in sympathetic tone (in response to vasodilation) counteracts the direct depressant effects on SA and AV nodal conduction. This renders felodipine ineffective in the treatment of supraventricular tachycardias.

Mutual Pharmaceutical generic pictured

Drug Characteristics: Felodipine

Dose Adjustment Hepatic	Liver failure, reduce dose to 2.5 mg po daily	**Absorption**	F = 13-20%, no food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 10 L/kg, protein binding 99%
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism, CYP3A4/5 substrate; moderate CYP2C8 inhibitor
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 26-33 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to felodipine	**Black Box Warnings**	None

Medication Safety Issues: Felodipine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew or crush SR tablet	No	Isordil, pindolol, Pletal, PriLOSEC, Prinivil	No

Drug Interactions: Felodipine

Typical Agents	Mechanism	Clinical Management
Amiodarone	Increased amiodarone concentrations and increased risk of bradycardia, heart block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
Beta-blockers	Increased risk of hypotension, bradycardia	Avoid concurrent use or monitor BP and HR
Clopidogrel	Decreased antiplatelet activity of clopidogrel by felodipine	Avoid concurrent use
CYP3A4/5 inhibitors	Decreased felodipine metabolism and increased risk of felodipine toxicity	Avoid concurrent use
CYP3A4/5 inducers	Increased felodipine metabolism and decreased felodipine efficacy	Monitor BP and consider dose increases of felodipine
CYP2C8 substrates	Decreased metabolism and increased risk of substrate toxicity	Monitor and consider a decrease substrate dose
Fentanyl	Increased risk of hypotension	Avoid concurrent use with felodipine

Adverse Reactions: Felodipine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Peripheral edema	Abdominal pain, arthralgia, constipation, dizziness, fatigue, f ushing, headache, hypotension, hyperkalemia, impotence, myalgia, nausea, palpitations, pruritus, rash, tachycardia, urticaria	Hepatotoxicity, thrombocytopenia

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema, increased heart rate, signs/symptoms of liver damage.

Key Patient Counseling Points. Report signs/symptoms of hypotension or exacerbation of angina with initial dosing and dose changes; report signs/symptoms of peripheral edema, fatigue, hypotension, or hepatic dysfunction. Do not drink alcohol while taking drug. Do not discontinue drug abruptly as this may cause rebound hypertension. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Dizziness may be worse if too much water is lost from the body due to excessive sweating, diarrhea, or vomiting.

Clinical Pearls. Dose can be reduced by one-half if taken consistently with grapefruit juice and monitoring for efficacy (BP, angina frequency) occurs.

FENOFIBRATE: Lofibra, Various

Global Pharmaceutical generic pictured

Class: Antihyperlipidemic

Dosage Forms. **Oral Tablet:** 35 mg, 40 mg, 48 mg, 54 mg, 105 mg, 145 mg, 160 mg; **Oral Capsule:** 30 mg, 43 mg, 50 mg, 67 mg, 130 mg, 134 mg, 150 mg, 200 mg; **Oral Capsule, Delayed Release:** 45 mg, 135 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypercholesterolemia, primary hypercholesterolemia, or mixed dyslipidemia (Frederickson type 2a, 2b): 160 mg po daily
2. Hypertriglyceridemia, Frederickson types 4 and 5 hyperlipidemia: 54-160 mg po daily

Off-Label Uses. None

MOA. Fibric acid derivatives activate peroxisome proliferator-activated receptor α (PPARα), which increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). The resulting fall in triglycerides produces an alteration in the size and composition of LDL from small, dense particles to large buoyant particles. These larger particles have a greater affinity for cholesterol receptors and are catabolized rapidly.

Drug Characteristics: Fenofibrate

Dose Adjustment Hepatic	Avoid use in severe hepatic impairment	**Absorption**	F = 60%, minimal food effect
Dose Adjustment Renal	Avoid use in severe renal impairment	**Distribution**	Vd = 60 L; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Prodrug that undergoes rapid hydrolysis at the ester bond to fenofibric acid. Fenofibric acid is glucuronidated in the liver
Pregnancy Category	C	**Elimination**	Renal elimination 60-93%, with a half-life of 24 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, gallbladder disease, severe renal or hepatic dysfunction, nursing mothers	**Black Box Warnings**	None

Medication Safety Issues: Fenofibrate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Capsules	No	Fibricor, Tracleer	No

Drug Interactions: Fenofibrate

Typical Agents	Mechanism	Clinical Management
Atorvastatin, HMG-CoA reductase inhibitors, colchicine	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use, or monitor for myopathy and consider dose reductions
Cholestyramine, colestipol	Decreased absorption of fenofibrate	Separate administration by 2 h
Ezetimibe	Increased ezetimibe concentrations and an increased risk of cholelithiasis	Avoid concurrent use or monitor for cholelithiasis
Glimeperide	Increased risk of hypoglycemia	Avoid concurrent use
Warfarin	Increased risk of bleeding	Monitor INR and consider dose adjustments

Adverse Reactions: Fenofibrate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hyperhomocysteinemia	Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea, rash, thrombophlebitis	Rhabdomyolysis, cholelithiasis, hepatotoxicity, mood disorder, impotence, agranulocytosis, nephrotoxicity, pancreatitis

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain; monitor LFT, CBC at baseline, 12 wk after initiation of therapy, or dose increases; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

Key Patient Counseling Points. Fenoglide tablets and Lipofen R capsules should be given with food; others can be taken without food. Take 1 h before or 4-6 h after a bile acid binding resin. Products are not interchangeable.

Clinical Pearls. The fibric acid derivatives (gemfibrozil, clofibrate, and fenofibrate) are recommended as alternatives to niacin in the treatment of types IIb, III, IV, and V hyperlipidemia. Gemfibrozil has less nephrotoxicity than other fibric acid derivatives. Clofibrate appears to have excess cardiovascular toxicity.

FENTANYL TRANSDERMAL: Duragesic, Various

Class: Opioid Analgesic. C-II

Dosage Forms. Transdermal Patch: 12 mcg/h, 25 mcg/h, 50 mcg/h, 75 mcg/h, 100 mcg/h

Common FDA Label Indication, Dosing, and Titration.

1. Pain, chronic (moderate to severe), Adults and Children >2 y of age: opioid tolerant, which cannot be managed by other means in opioid-tolerant patients, transdermal fentanyl dosage based on the patient's current 24-h oral morphine requirement; replace patch q72h; may replace patch q48h in patients not achieving adequate analgesia

Off-Label Uses. None

MOA. Fentanyl is a phenylpiperidine opioid agonist with predominant effects on the mu opioid receptor and is about 50-100 times more potent as an analgesic than morphine.

Duragesic by Pricara 50 mcg/h pictured

Drug Characteristics: Fentanyl Transdermal

Dose Adjustment Hepatic	Not required	**Absorption**	F = 92% with transdermal
Dose Adjustment Renal	CrCl <10 mL/min, reduce dose by 50%	**Distribution**	Vd = 6 L/kg; 80-85% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	75% renal elimination, half-life of 20-24 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Acute or postoperative pain, bronchial asthma, hypersensitivity to fentanyl, mild or intermittent pain management, opioid nontolerant patients, paralytic ileus	**Black Box Warnings**	CYP3A4/5 inhibitors; respiratory depression; transdermal not for use post-op; fatalities in children; formulations not interchangeable; fever; care with disposal; REMS program

Medication Safety Issues: Fentanyl Transdermal

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Suffix describes mcg/h of fentanyl delivered. Transdermal fentanyl patches should always be prescribed in mcg/h, not size	FentaNYL	No	Yes	Alfentanil, SUFentanil	No

Drug Interactions: Fentanyl Transdermal

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Beta-blockers and calcium channel blockers	Additive hypotension when combined with fentanyl anesthesia	Avoid concurrent use
Buprenorphine, opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use of opioid antagonists and opioid agonists
CYP3A4/5 inducers	Increased fentanyl metabolism decreases fentanyl efficacy	Consider dose increases of fentanyl
CYP3A4/5 strong/moderate inhibitors	Decreased fentanyl metabolism increases risk of fentanyl toxicity	Avoid concurrent use
MAOIs	Additive respiratory depression	Avoid concurrent use

Adverse Reactions: Fentanyl Transdermal

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Application site reactions, sweating, constipation, GI distress, confusion, headache, anxiety, urinary retention, upper respiratory tract infection, fatigue	Arrhythmias, chest pain, dyspnea, respiratory depression	Stevens-Johnson syndrome, physical dependence, tolerance

Efficacy Monitoring Parameters. Relief of pain.

Toxicity Monitoring Parameters. Severe skin rash, excessive drowsiness, decreased breathing, severe constipation, chest pain, inability to urinate, constipation.

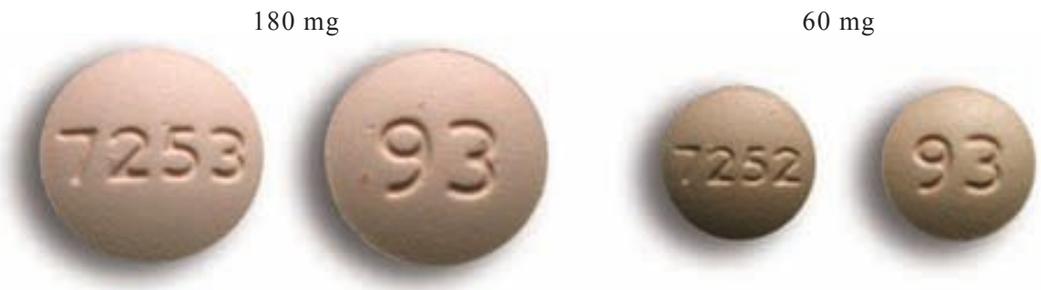
Key Patient Counseling Points. Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Apply to clean, dry skin. Skin breaks may increase absorption. Remove old patch when new patch applied. Febrile patients may have increased absorption. Monitor carefully.

Clinical Pearls. Use caution in elderly, appear more sensitive to the effects. Tolerance and physical dependence may occur with chronic use, avoid abrupt discontinuation. Significant addiction potential, care with storage and disposal. In an REMS program, provide medication guide. Substantial differences exist in the pharmacokinetic profile of fentanyl products. Do not convert patients on a mcg-per-mcg basis from one fentanyl product to another fentanyl product; the substitution of one fentanyl product for another fentanyl product may result in a fatal overdose. Do not cut patch. Contraindicated in opioid-naïve patients; use limited to opioid tolerant patients.

FEXOFENADINE: Allegra, Various

Class: Antihistamine

Dosage Forms. **Oral Tablet**: 30 mg, 60 mg, 180 mg; **Oral Disintegrating Tablet:** 30 mg; **Oral Suspension:** 30 mg/5 mL



Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Seasonal allergic rhinitis (OTC): Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily
2. Idiopathic urticaria: Children 6 mo-2 y of age, 15 mg po bid; Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily

Off-Label Uses.

1. Perennial allergic rhinitis: Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily

MOA. Fexofenadine, the major active metabolite of terfenadine, is an antihistamine with selective peripheral H_1-receptor antagonist activity. Both enantiomers of fexofenadine displayed approximately equipotent antihistaminic effects.

F

Drug Characteristics: Fexofenadine

Dose Adjustment Hepatic	Not required	**Absorption**	Rapidly absorbed, bioavailability not established
Dose Adjustment Renal	Use with caution	**Distribution**	Vd = 5.4-5.8 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Little hepatic or extrahepatic metabolism
Pregnancy Category	C	**Elimination**	Fecal elimination is 80% with a half-life of 14-18 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to fexofenadine	**Black Box Warnings**	None

Medication Safety Issues: Fexofenadine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not split or chew disintegrating tablet	No	Viagra	No

Drug Interactions: Fexofenadine

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Possible increase in sedation effects	Use with caution, monitor for sedation
Antacids	Aluminum or magnesium containing products reduce the bioavailability of fexofenadine	Separate administration by 2 h

Adverse Reactions: Fexofenadine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Sedation, dry mouth, fatigue, and nausea	Hypersensitivity, insomnia

Efficacy Monitoring Parameters. Improvement in rhinitis or urticaria symptoms.

Toxicity Monitoring Parameters. Seek medical attention for signs of severe CNS toxicity.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Take the suspension with water only, shake well before use. The oral disintegrating tablet should be taken on an empty stomach and stored in the blister pack until used. Place on tongue and allow to dissolve, do not crush or chew. Can be swallowed with water but not with fruit juices.

Clinical Pearls. Product is available OTC in several additional dosage forms.

FIDAXOMICIN: Dificid

Class: Macrolide Antibiotic

Dosage Forms. Oral Tablet: 200 mg

Common FDA Label Indication, Dosing, and Titration.

1. *C. difficile* infection: 200 mg po bid × 10 d

Off-Label Uses. None

MOA. Fidaxomicin is an antibacterial agent that acts locally in the GI tract on *C. difficile* via inhibition of RNA polymerases.

Optimer 200 mg pictured

Drug Characteristics: Fidaxomicin

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal oral bioavailability, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed systemically
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	B	**Elimination**	Fecal >92% unchanged with half-life of 11.7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	None	**Black Box Warnings**	None

Medication Safety Issues: Fidaxomicin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Fidaxomicin. None known

Adverse Reactions: Fidaxomicin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea	Abdominal pain, vomiting, anemia, neutropenia	Bowel obstruction, GI hemorrhage

Efficacy Monitoring Parameters. Resolution of symptoms of *C. difficile* infection, including resolution of diarrhea, vomiting.

Toxicity Monitoring Parameters. Monitor for signs of bowel obstruction and blood in the stool.

Key Patient Counseling Points. May be given with or without food.

Clinical Pearls. Expensive alternative to oral vancomycin for management of *C. difficile*–associated diarrhea. Minimally absorbed; can not be used for systemic infections.

FINASTERIDE: Proscar, Propecia, Various

Class: 5α-Reductase Inhibitor

Dosage Forms. Oral Tablet: 1 mg, 5 mg

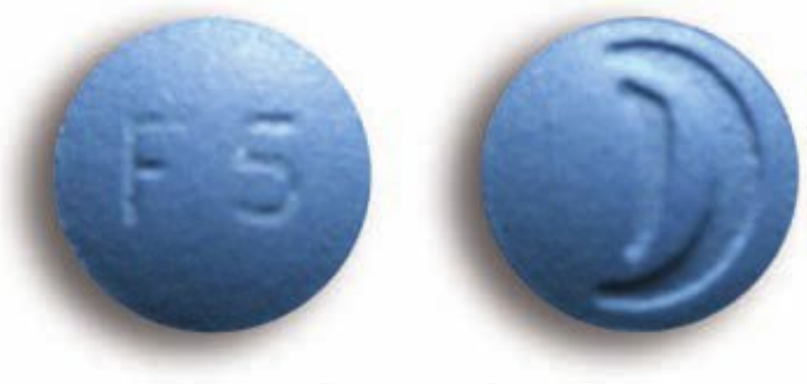
Common FDA Label Indication, Dosing, and Titration.

1. Benign prostatic hyperplasia: 5 mg po daily
2. Male pattern alopecia: 1 mg po daily

Off-Label Uses.

1. Prostate cancer prevention: 5 mg po daily

MOA. Finasteride inhibits the conversion of testosterone to 5α-dihydrotestosterone (DHT) by 5α-reductase, isoform 2.



Northstar Rx generic 5 mg pictured

Drug Characteristics: Finasteride

Dose Adjustment Hepatic	Not required	**Absorption**	F = 63%, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 76 L; 90% protein bound
Dialyzable	Unknown	**Metabolism**	<20% hepatic, CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Renal clearance is 40% with a half-life of 6 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to finasteride, pregnancy, children	**Black Box Warnings**	None

Medication Safety Issues: Finasteride

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	ProSom, Provera, PROzac	No

Drug Interactions: Finasteride. None known

Adverse Reactions: Finasteride

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Impotence, reduced libido	Gynecomastia, dizziness	Heart failure, angioedema, allergic skin reactions, male breast cancer

Efficacy Monitoring Parameters. American Urologic Association (AUA) Symptom Score, decrease in residual urine volume, increased urine flow if using for BPH; increased hair growth if using for male pattern alopecia.

Toxicity Monitoring Parameters. Shortness of breath, swelling, breast pain, or mass.

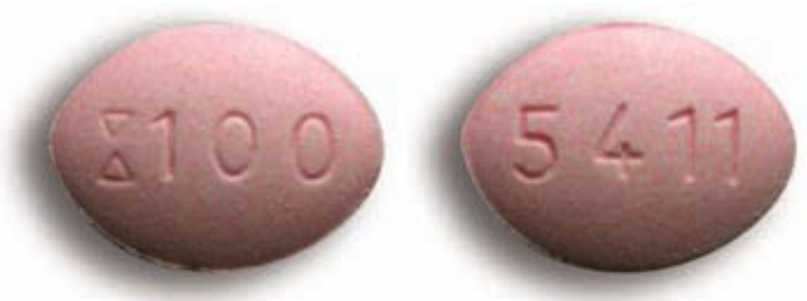
Key Patient Counseling Points. For hair loss, you may need to take this medicine for 3 mo or longer before you see an effect. For an enlarged prostate, you may need to take this medicine for up to 6 mo to see the full effect. Women who are pregnant or may become pregnant should avoid touching or handling this medicine. This medicine can get into the body through the skin and may prevent development of genitalia in an unborn male baby. They should also avoid semen of a man taking finasteride.

Clinical Pearls. Not effective for the treatment of prostate cancer. Is effective in reducing the overall incidence of prostate cancer, although an increase in the incidence of high-grade prostate cancers has been observed. Draw baseline PSA before initiating therapy. Note that PSA will decrease by 50% with treatment, double PSA values when assessing for prostate cancer. Does not affect free PSA level. Hazardous agent: Use appropriate precautions for handling and disposal.

FLUCONAZOLE: Diflucan, Various

Class: Imidazole Antifungal

Dosage Forms. **Powder for Oral Suspension:** 10 mg/mL, 40 mg/mL; **Oral Tablet:** 50 mg, 100 mg, 150 mg, 200 mg



Teva generic 100 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Candidal vulvovaginitis, uncomplicated: 150 mg po × 1
2. Candidal vulvovaginitis, complicated: 150 mg po q72h × 3 doses
3. Candidiasis: systemic: Adults, 400 mg po daily; Children ≥6 mo of age, 6-12 mg/kg/d po
4. Cryptococcal meningitis: Adults, 400-800 mg po daily × 8 wk, then 200 mg po daily × 6-12 mo; Children ≥6 mo of age, 12 mg/kg po on day 1, then 6 mg/kg/d (*max* 12 mg/kg/d) for 10-12 wk
5. Oropharyngeal candidiasis: Adults, 100-200 mg po daily × 7-14 d; Children ≥6 mo of age, 6 mg/kg po on day 1, then 3 mg/kg once daily for at least 2 wk

Off-Label Uses.

1. Onychomycosis due to dermatophyte: 200 mg po qwk × 3 mo (fingernails), × 6 mo (toenails)
2. Tinea: 200 mg po qwk × 3 doses

F

MOA. Fluconazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability.

Drug Characteristics: Fluconazole

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90% with no food effect
Dose Adjustment Renal	Not required for single-dose therapy; for repeated dose therapy, CrCl 21-50 mL/min, increase dosing interval to 48 h or decrease dose by 50%; CrCl <10 mL/min, extend dosing interval to 48 h and decrease dose by 50%	**Distribution**	Blister, CSF, nails, skin, saliva, sputum, vaginal tissue, urine
Dialyzable	100% of dose is removed by hemodialysis	**Metabolism**	Minimal metabolism, but moderate inhibitor of CYP2C19, CYP3A4/5 and strong inhibitor of CYP2C9
Pregnancy Category	C	**Elimination**	80% of dose is eliminated renally unchanged, half-life of 30 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to f uconazole, concurrent ergot alkaloids, CYP3A4/5 substrates that prolong QT	**Black Box Warnings**	None

Medication Safety Issues: Fluconazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Flecainide, FLUoxetine, furosemide, itraconazole, voriconazole	No

Drug Interactions: Fluconazole

Typical Agents	Mechanism	Clinical Management
Agents that prolong QT interval	Increased risk of QT prolongation	Avoid concurrent use; astemizole and cisapride are contraindicated
Atorvastatin, HMG-CoA reductase inhibitors	Increased risk of rhabdomyolysis	Monitor for signs and symptoms of myopathy or rhabdomyolysis
CYP2C19, CYP2C9, CYP3A4/5 substrates	Decreased metabolism of substrates and increased substrate toxicity	Avoid concurrent use if possible; monitor and consider dose reductions of substrates
Sulfonylureas	Increased risk of hypoglycemia	Avoid concurrent use; monitor and consider dose reductions

Adverse Reactions: Fluconazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea	Stevens-Johnson syndrome, arrhythmias, adrenal suppression, agranulocytosis, seizures, elevated LFTs, hypokalemia

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Severe skin irritation or rash, unusual bruising or bleeding, rapid heart beat, yellowing of the eyes or skin; monitor serum potassium.

Key Patient Counseling Points. Many medications, including OTC medications, interact with fluconazole. Do not take any new medications without consulting your doctor or pharmacist. If taking a weekly dose, take on same day and time each week.

Clinical Pearls. Oral and IV doses are interchangeable. Amphotericin is more effective than fluconazole in treating serious fungal infections; fluconazole is typically used as adjunctive therapy or maintenance therapy. In vaginal candidiasis, single-dose fluconazole is at least as effective as a 5-d course of oral ketoconazole or a 3-d course of intravaginal clotrimazole.

FLUOCINONIDE TOPICAL: Lidex, Various

Class: Topical Corticosteroid

Dosage Forms. **Topical Cream:** 0.05%, 0.1%; **Topical Ointment:** 0.05%; **Topical Solution:** 0.05%; **Topical Gel:** 0.05%

Common FDA Label Indication and Dosing.

1. Skin disorders, corticosteroid responsive: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2 wk
2. Plaque psoriasis: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2-4 wk
3. Atopic dermatitis: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2 wk

Off-Label Uses.

1. Oral lichen planus: Apply thin layer topically bid with antimycotics

MOA. Fluocinonide is an anti-inflammatory, antipruritic, and vasoconstrictive corticosteroid. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Teva generic 0.05% ointment pictured

F

Drug Characteristics: Fluocinonide

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption unless covering large surface area or covering areas lacking skin integrity
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to f uocinonide or other corticosteroids	**Black Box Warnings**	None

Medication Safety Issues: Fluocinonide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Lasix, Videx	No

Drug Interactions: Fluocinonide. None known

Adverse Reactions: Fluocinonide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dry skin, burning sensation, stinging, pruritus at site of administration; headache	HPA suppression has been reported when used with occlusive dressings over larger surface areas

Efficacy Monitoring Parameters. Improvement in clinical signs of skin disorder (reduced inflammation, pruritus).

Toxicity Monitoring Parameters. Severe skin irritation or symptoms worsen after administration.

Key Patient Counseling Points. Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

Clinical Pearls. High-potency corticosteroid. Application to large surface areas, prolonged use, and use of occlusive dressings increases risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption. Other corticosteroid-containing products are available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects.

FLUOXETINE: Prozac, Various

Class: SSRI Antidepressant

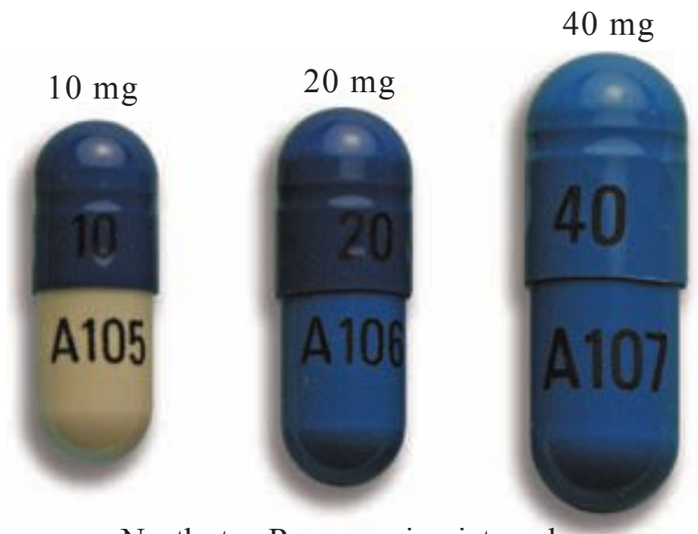
Dosage Forms. **Oral Capsule:** 10 mg, 20 mg, 40 mg; **Oral Capsule, Delayed Release, Weekly:** 90 mg; **Oral Tablet:** 10 mg, 20 mg, 60 mg; **Oral Solution, Oral Syrup:** 20 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Adults and Children ≥8 y of age, 20 mg po daily; may titrate to 80 mg po daily
2. OCD: Adults, 20 mg po daily, may titrate to 80 mg po daily; Children ≥7 y of age, 10 mg po daily, may titrate to 30 mg po daily
3. Panic disorder: 10 mg po daily, may increase to 60 mg po daily
4. Premenstrual dysphoric disorder: 20 mg po daily or for 14 d prior to expected start of menses; may titrate to 80 mg po daily

Off-Label Uses.

1. Posttraumatic stress disorder: 20-80 mg po daily
2. Fibromyalgia: 20-80 mg po daily



Northstar Rx generic pictured

MOA. Fluoxetine is a bicyclic antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI).

Drug Characteristics: Fluoxetine

Dose Adjustment Hepatic	Use lower dose	**Absorption**	F = 100%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 12-43 L/kg; 95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic, CYP2C9 and CYP2D6 substrate; strong CYP2D6 inhibitor, moderate 2C19 inhibitor
Pregnancy Category	C	**Elimination**	Renal elimination 60% with half-life of 4-6 d
Lactation	Avoid	**Pharmacogenetics**	Use caution in CYP2D6 poor metabolizers
Contraindications	Hypersensitivity; concomitant pimozide, thioridazine, or MAOIs	**Black Box Warnings**	Suicidality; approved in children >7 y

Medication Safety Issues: Fluoxetine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
PROzac Weekly	FLUoxetine, PROzac	ER capsule	No	Paxil, Prelone, PriLOSEC, Prograf, Proscar, ProSom	No

Drug Interactions: Fluoxetine

Typical Agents	Mechanism	Clinical Management
Antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Agents that prolong the QT interval	Increased risk of QT prolongation, torsades de pointes, cardiac arrest	Avoid concurrent use
CYP2C9 and CYP2D6 substrates	Decreased metabolism of substrates, increased substrate toxicity	Monitor for adverse effects; consider dose reductions. Avoid concurrent use if narrow therapeutic index medication
CYP2C9 inducers	Increased metabolism of fluoxetine and decreased fluoxetine efficacy	Monitor for efficacy and consider dose increases of fluoxetine
CYP2C9 and CYP2D6 inhibitors	Decreased metabolism of fluoxetine and increased risk of fluoxetine toxicity	Avoid concurrent use if strong inhibitor; for moderate inhibitors, monitor for fluoxetine toxicity and consider dose decreases of fluoxetine
Triptans, dextroamphetamine, tramadol, linezolid, MAOIs	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome; linezolid, MAOIs contraindicated

Adverse Reactions: Fluoxetine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, headache, nausea, somnolence, tremor, xerostomia	Anxiety, asthenia, bleeding, diaphoresis, disorder of ejaculation, fatigue, insomnia, loss of appetite, rash, sexual dysfunction, weight gain	Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsade de pointes

Efficacy Monitoring Parameters. Improvement in symptoms of depression, panic disorder, OCD, premenstrual syndrome.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

Key Patient Counseling Points. Take without meals and in the morning. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

Clinical Pearls. If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Must be dispensed with medication guide. Weekly dosage form with more pharmacokinetic variability than daily dosing. If stable on 20 mg daily, can be converted to 90 mg weekly dose, starting 7 d after the last 20 mg dose.

FLUTICASONE NASAL INHALER: Flonase, Various

Class: Intranasal Adrenal Glucocorticosteroid

Dosage Forms. **Nasal Spray:** 27.5 mcg/actuation, 50 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Allergic rhinitis: Children ≥4 y of age and Adults, 2 sprays/nostril daily or 1 spray/nostril bid; *max* of 2 sprays/nostril/d (200 mcg/d)
2. Nonallergic rhinitis: Children ≥4 y of age and Adults, 2 sprays/nostril daily or 1 spray/nostril bid; *max* of 2 sprays/nostril/d (200 mcg/d)

Off-Label Uses.

1. Adjunct to antibiotics in empiric treatment of acute bacterial rhinosinusitis: 1 spray/nostril bid

MOA. Fluticasone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Apotex Corp generic 50 mcg pictured

F

Drug Characteristics: Fluticasone Nasal Inhaler

Dose Adjustment Hepatic	Not required	**Absorption**	<2% of dose absorbed systemically after nasal administration
Dose Adjustment Renal	Not required	**Distribution**	Vd approximately 4 L/kg after nasal administration
Dialyzable	Not dialyzable	**Metabolism**	Complete first-pass metabolism
Pregnancy Category	C	**Elimination**	Primarily fecal elimination with half-life (calculated from IV dose) of 5-7 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Fluticasone Nasal Inhaler

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Flovent	No

Drug Interactions: Fluticasone Nasal Inhaler

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased f uticasone metabolism and increased risk of f uticasone toxicity	Monitor for toxicity; reduce dose of f uticasone if necessary

Adverse Reactions: Fluticasone Nasal Inhaler

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nasal irritation and burning	Epistaxis	Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis

Efficacy Monitoring Parameters. Control of rhinitis signs and symptoms.

Toxicity Monitoring Parameters. While only small amounts of fluticasone reach systemic circulation, bone mineral density and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection.

Key Patient Counseling Points. Advise patients on the proper administration technique for this product. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

Clinical Pearls. Oral inhalation and topical dosage forms of fluticasone also available for treatment of other allergic disorders. While oral antihistamines (either OTC or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects.

FLUTICASONE ORAL INHALER: Flovent HFA

GlaxoSmithKline pictured

Class: Inhaled Adrenal Corticosteroid

Dosage Forms. **Metered Dose Inhaler**: 44 mcg/actuation, 110 mcg/actuation, 220 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Asthma: Children 4-11 y of age, regardless of previous treatment, starting dose 88 mcg bid with *max* dose of 88 mcg bid; Children ≥12 y of age and Adults: Patients previously treated with inhaled bronchodilators alone, 88 mcg bid, titrate dose to response with maximum of 440 mcg bid; Patients previously treated with inhaled corticosteroids, starting dose 88-220 mcg bid; titrate dose to response with *max* of 440 mcg bid; Patients previously treated with oral corticosteroids, starting dose 440 mcg bid; titrate dose to response with *max* of 880 mcg bid

Off-Label Uses. None

MOA. Fluticasone is a synthetic trifluorinated corticosteroid with anti-inflammatory effects. It is a human glucocorticoid receptor agonist that inhibits multiple cell types and mediator production or secretion involved in asthma. Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids, cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

Drug Characteristics: Fluticasone Oral Inhaler

Dose Adjustment Hepatic	Not required	**Absorption**	F = 18-30% after MDI administration
Dose Adjustment Renal	Not required	**Distribution**	Vd ~4 L/kg after oral inhalation
Dialyzable	Not dialyzable	**Metabolism**	Complete first-pass metabolism via CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is <5% with a half-life of 11-12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity or severe allergy to milk proteins (included in the inhalation powder); should not be used for primary treatment of status asthmaticus or other acute episodes of asthma requiring intensive intervention	**Black Box Warnings**	None

Medication Safety Issues: Fluticasone Oral Inhaler

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
HFA	No	No	No	Flonase	No

Drug Interactions: Fluticasone Oral Inhaler

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased fluticasone metabolism and increase risk of fluticasone toxicity	Monitor for toxicity; reduce dose of fluticasone if necessary

Adverse Reactions: Fluticasone Oral Inhaler

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Pharyngeal candidiasis	Epistaxis	Severe hypersensitivity, glaucoma, cataracts, pneumonia, secondary hypocortisolism; osteoporosis

Efficacy Monitoring Parameters. Control of asthma symptoms, as measured by PFTs.

Toxicity Monitoring Parameters. While only small amounts of fluticasone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection (including oral candidiasis).

Key Patient Counseling Points. Proper administration technique for these inhaled products. Instruct on rinsing mouth with water after each use to prevent oral infections. Monitor for signs of toxicity, especially adrenal insufficiency, oral candidiasis, and worsening pulmonary function.

Clinical Pearls. Flovent Diskus product also available for the treatment of asthma; delivers fluticasone in powder form with dosing similar to the metered dose inhaler formulation. Intranasal and topical dosage forms of fluticasone also available for treatment of other allergic disorders.

FLUTICASONE/SALMETEROL: Advair Diskus, Advair HFA

GlaxoSmithKline 250 mcg/50 mcg pictured

Class: Inhaled Corticosteroid and Long-Acting β_2-Adrenergic Agonist Combination

Dosage Forms. Inhalation Disk: 100/50 (fluticasone 0.1 mg plus salmeterol 0.05 mg/actuation), 250/50 (fluticasone 0.25 mg plus salmeterol 0.05 mg/actuation), 500/50 (fluticasone 0.5 mg plus salmeterol 0.05 mg/actuation); **Metered Dose Inhaler (MDI):** 45/21 (fluticasone 45 mcg plus salmeterol 21 mcg/actuation), 115/30.45 (fluticasone 115 mcg plus salmeterol 21 mcg/actuation), 230/21 (fluticasone 230 mcg plus salmeterol 21 mcg/actuation)

Common FDA Label Indication, Dosing, and Titration.

1. Asthma: 1 disk or 2 MDI puffs q12h, adjust dose to patient response
2. Chronic obstructive pulmonary disease (COPD): 1 disk q12h, adjust dose to patient response

Off-Label Uses. None

MOA. Fluticasone is a synthetic trifluorinated corticosteroid with anti-inflammatory effects. It is a human glucocorticoid receptor agonist that inhibits multiple cell types and mediator production or secretion involved in asthma and COPD. Salmeterol is a long-acting β_2-adrenergic agonist, stimulates intracellular adenyl cyclase in catalyzing the conversion of adenosine triphosphate (ATP) to cyclic-3′,5′-adenosine monophosphate (cyclic AMP). The increased cyclic AMP levels result in the relaxation of bronchial smooth muscle and inhibition of the release of mediators of instantaneous hypersensitivity from mast cells.

F

Drug Characteristics: Fluticasone/Salmeterol

Dose Adjustment Hepatic	Not required	**Absorption**	After inhalation, f uticasone F = 18% and salmeterol is undetectable
Dose Adjustment Renal	Not required	**Distribution**	Both f uticasone and salmeterol are largely (>90%) protein bound
Dialyzable	Not dialyzable	**Metabolism**	Fluticasone undergoes complete first-pass metabolism; salmeterol is extensively metabolized in the liver by CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is <5% for both components; f uticasone half-life after inhalation of 5-7 h, salmeterol half-life after oral administration of 5.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to any component of the product, including milk proteins (included in the inhalation powder); should not be used as primary treatment of status asthmaticus or acute episodes of asthma or COPD, posaconazole coadministration	**Black Box Warnings**	Increased asthma related deaths

Medication Safety Issues: Fluticasone/Salmeterol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
HFA	No	No	No	Adcirca, Advicor	No

Drug Interactions: Fluticasone/Salmeterol

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased fluticasone metabolism and increase risk of fluticasone toxicity	Monitor for toxicity; reduce dose of fluticasone if necessary

Adverse Reactions: Fluticasone/Salmeterol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, pharyngitis, upper respiratory infection, difficulty speaking	Nausea, oral candidiasis, musculoskeletal pain, throat irritation, bronchitis, dizziness	Atrial fibrillation, myocardial infarction, anaphylaxis, osteoporosis, bronchospasm, exacerbation of asthma, paradoxical bronchospasm

Efficacy Monitoring Parameters. Control of asthma or COPD symptoms, as measured by PFTs.

Toxicity Monitoring Parameters. While only small amounts of fluticasone and almost no salmeterol reach systemic circulation, bone mineral density and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection (including oral candidiasis).

Key Patient Counseling Points. Proper administration technique for these inhaled products; rinse mouth with water after each use to prevent oral infections. Monitor for signs of toxicity, especially adrenal insufficiency, oral candidiasis, and worsening pulmonary function.

Clinical Pearls. Long-acting β_2-agonists (LABAs), such as salmeterol, increase the risk of asthma-related deaths; fluticasone and salmeterol should only be used in patients not adequately controlled on a long-term asthma control medication (ie, inhaled corticosteroid) or whose disease severity requires initiation of 2 maintenance therapies. Once asthma control is achieved and maintained, discontinue fluticasone/salmeterol if possible without loss of asthma control and maintain the patient on a long-term asthma control medication. Medication guide required at dispensing.

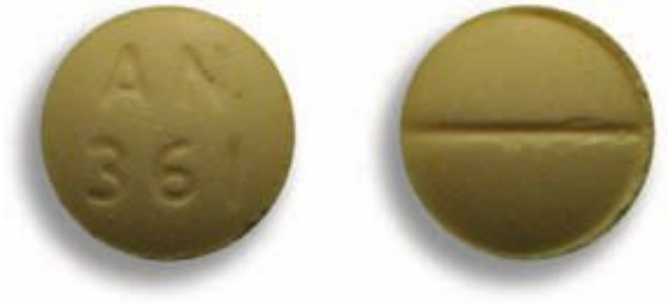
FOLIC ACID: Folacin-800, Various

Class: Essential B Vitamin

Dosage Forms. **Oral Tablet:** 0.4 mg, 0.8 mg, 1 mg; **Oral Capsule:** 0.8 mg, 5 mg, 20 mg

Common FDA Label Indication, Dosing, and Titration.

1. Folic acid deficiency: Adults, 0.4-1 mg po daily; Children, infants, 0.1 mg/d; Children age <4 y, up to 0.3 mg/d; Children ≥age 4 y of age, 0.4-1 mg/d
2. Pregnancy, prophylaxis: 0.4-1 mg po daily



Amneal generic 1 mg pictured

Off-Label Uses.

1. Prevention of neural tube defects: 4 mg po daily
2. Prevention of methotrexate toxicity: 5-27.5 mg po weekly

MOA. Folic acid is required for the conversion of deoxyuridylate to thymidylate, which is a rate-limiting step in DNA synthesis, which presents clinically as macrocytic anemia when red blood cells are unable to extrude their nucleus.

Drug Characteristics: Folic Acid

Dose Adjustment Hepatic	Not required	**Absorption**	F = 76-93%
Dose Adjustment Renal	Not required	**Distribution**	Stored in the liver and most tissues
Dialyzable	Yes, hemodialysis	**Metabolism**	Metabolized in the liver to active metabolite, 5-methyltetrahydrofolate
Pregnancy Category	A	**Elimination**	Renal = 30%
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Folic Acid

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Folinic acid	No

Drug Interactions: Folic Acid

Typical Agents	Mechanism	Clinical Management
Barbiturates	Decreased folic-acid absorption; increased barbiturate metabolism and less efficacy	Monitor barbiturate efficacy
Phenytoin	Decreased folic-acid serum levels; decreased phenytoin effectiveness	Monitor for seizure control

Adverse Reactions: Folic Acid

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Loss of appetite	Confusion, irritation	Anaphylaxis

Efficacy Monitoring Parameters. B_{12} and folic acid levels, normalization of MCV, normalization of Hgb, resolution of symptoms of anemia (fatigue, shortness of breath). Absence of neural tube defects in newborns.

Toxicity Monitoring Parameters. Seek medical attention if severe shortness of breath, skin rash, or hives.

Key Patient Counseling Points. May require several weeks for maximum effect. Avoid alcohol as it inhibits the absorption of folic acid.

Clinical Pearls. Drugs that interfere with folate metabolism (methotrexate, hydroxyurea, pemetrexed) will cause an elevated MCV in the absence of vitamin B deficiency. Folic acid is given to women intending to become pregnant and in the early months of pregnancy to reduce the risk of neural tube defects and other birth defects (imperforate anus, cleft lip). Patients on pemetrexed receive folic acid to reduce pemetrexed toxicity. Enriched flour, bread, corn meal, pasta, rice, and other grain products have added folic acid to help decrease the risk of neural tube defects by increasing folic acid intake. Other foods that contain folic acid include dark green leafy vegetables, citrus fruits and juices, and lentils.

FOSINOPRIL: Monopril, Various

Class: ACE-I, Antihypertensive

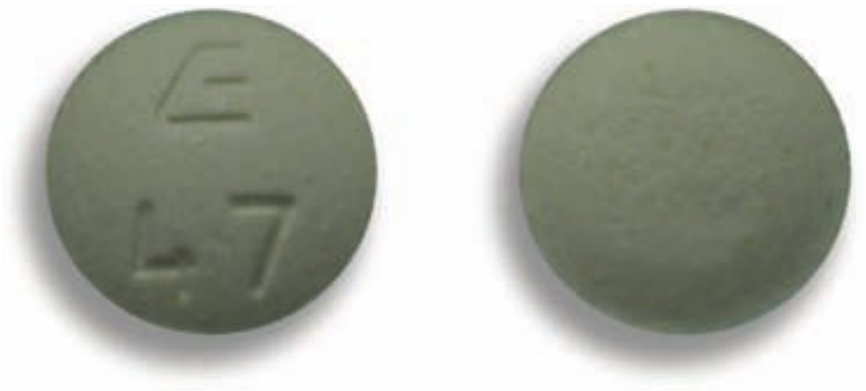
Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: 5-10 mg po daily, may titrate to 40 mg po daily
2. Hypertension: Adults, 10 mg po daily, may titrate to 80 mg po daily; Children 6-16 y of age and weighing >50 kg, 5-10 mg po daily, may titrate to 40 mg po daily

Off-Label Uses. None

MOA. Fosinopril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.



Sandoz generic 40 mg pictured

Drug Characteristics: Fosinopril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 36%, food decreases rate (not extent) of absorption
Dose Adjustment Renal	CrCl = 10-30 mL, 5 mg po daily; CrCl <10 mL/min, 2.5 mg daily	**Distribution**	99% protein bound
Dialyzable	Removed by hemodialysis	**Metabolism**	Metabolized in liver to active metabolite (fosinoprilat) not via CYP450
Pregnancy Category	C (1st trimester), D (2nd and 3rd trimesters)	**Elimination**	50% renal elimination with a half-life of 12 h (fosinoprilat)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, history of ACEI-induced angioedema, and hereditary or idiopathic angioedema	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Fosinopril

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	FLUoxetine, Fosamax, furosemide, lisinopril	No

Drug Interactions: Fosinopril

Typical Agents	Mechanism	Clinical Management
Antacids	Binding and decreased absorption	Separate administration by 2 h
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Angiotensin receptor blockers	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive effect of fosinopril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels
Aliskiren	Increased risk of hyperkalemia	Monitor serum potassium levels
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use; monitor for anemia or leukopenia
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly

Adverse Reactions: Fosinopril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness	Diarrhea, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting	Angioedema, birth defects, liver failure

Efficacy Monitoring Parameters. Decreased BP, decrease in signs of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

Key Patient Counseling Points. Full effect may require 2-4 wk. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

Clinical Pearls. Observe patients who are volume depleted for at least 2 h after taking the initial dose of fosinopril. Discontinue if renal deterioration occurs.

FUROSEMIDE: Lasix, Various

Class: Loop Diuretic

Dosage Forms. Oral Tablet: 20 mg, 40 mg, 80 mg; **Oral Solution:** 8 mg/1 mL, 10 mg/1 mL

Ranbaxy generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Edema related to heart failure, renal failure: Adults, initial 20-80 mg po daily, may titrate to maintenance dose (*max* 600 mg/d); Premature neonates (<29 wk), 1-2 mg/kg/dose po daily, may titrate to 6 mg/kg/dose; Premature neonates (>29 wk), 1-2 mg/kg/dose po 1-2 times per day, may titrate to 6 mg/kg/dose; Neonates, 1-3 mg/kg po q8h as needed; Infants and Children, initial, 2 mg/kg/dose po, may titrate at intervals of 6-8 h to maintenance dose (*max* 6 mg/kg/dose)
2. Hypertension: Adults, 40 mg po BID, may titrate to patient response; Children, 0.5-2 mg/kg/dose po once or twice daily; Infants <6 mo of age, may require doses up to 3 mg/kg po daily in 2 divided doses; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d

Off-Label Uses. None

MOA. Furosemide is a loop diuretic that is actively secreted via the nonspecific organic acid transport system into the lumen of the thick ascending limb of Henle's loop, where it decreases sodium reabsorption by competing for the chloride site on the Na^+-K^+-$2Cl^-$ cotransporter.

F

Drug Characteristics: Furosemide

Dose Adjustment Hepatic	Not required, patients with hepatic failure may need higher doses to achieve diuresis	**Absorption**	F = 47-70%, food may lower Cmax and Tmax
Dose Adjustment Renal	Not required, patients with renal failure may need higher doses to achieve diuresis	**Distribution**	Protein binding 91-99%
Dialyzable	Not dialyzable	**Metabolism**	Minimal hepatic metabolism (10%)
Pregnancy Category	C	**Elimination**	Eliminated 60-90% unchanged in urine, 7-9% in feces, and 6-8% in bile, with a half-life of 30-120 min
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to furosemide; anuria	**Black Box Warnings**	Fluid and electrolyte loss

Medication Safety Issues: Furosemide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Lanoxin, Lidex, Lomotil, Lovenox, Luvox	No

Drug Interactions: Furosemide

Typical Agents	Mechanism	Clinical Management
ACE-Is	Increased risk of postural hypotension (first dose)	Start with low dose of ACE-I and monitor BP
Aminoglycosides	Increased aminoglycoside serum concentrations, additive ototoxicity and/or nephrotoxicity	Avoid concomitant use; monitor SCr and hearing
Antidiabetic drugs	Decreased hypoglycemic effect	Monitor blood glucose levels
Antiarrhythmic agents, digoxin	Increased risk of ventricular arrhythmias (torsade de pointes) due to hypokalemia, hypomagnesemia	Monitor serum potassium and magnesium levels; supplement electrolytes
Bile acid resins	Decreased furosemide efficacy	Give cholestyramine 4 h after furosemide; monitor diuretic effect
Diuretics	Increased diuretic response to furosemide	Monitor serum electrolytes and SCr
Lithium	Increased lithium concentrations and risk of toxicity	Decrease lithium dose and monitor serum lithium levels
NSAIDs	Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels

Adverse Reactions: Furosemide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hyperuricemia	Asthenia, constipation, headache, hyperglycemia, hypocalcemia, hypokalemia, hypomagnesemia, muscle spasm, orthostatic hypotension, rash, vomiting	Nephrotoxicity, ototoxicity, thrombocytopenia, tinnitus

Efficacy Monitoring Parameters. Decreased BP, increased urine output, reduction in edema, daily weights. For treating renal failure, increase in urine volume, CrCl, BUN, and electrolytes.

Toxicity Monitoring Parameters. Severe volume depletion can occur. Monitor serum and urine electrolytes, uric acid, and blood glucose at baseline and every 3-6 mo after therapy. Audiometric test (if ototoxicity suspected).

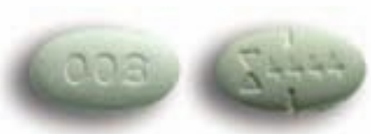
Key Patient Counseling Points. Avoid alcohol and NSAIDs. Increased risk of sun sensitivity; use sunscreen and avoid tanning. Avoid activities requiring coordination until drug effects are realized, as drug may cause dizziness, vertigo, or blurred vision. Report signs/symptoms of hypotension, decreased urine output, or ototoxicity; severe skin reactions. Eat high-potassium foods, as directed by health-care professional.

Clinical Pearls. Drug of first choice for edema.

GABAPENTIN: Neurontin, Gralise, Various

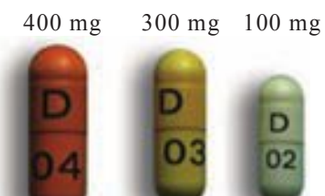
Class: Gamma Aminobutyric Acid, Anticonvulsant

Dosage Forms. Oral Capsule: 100 mg, 300 mg, 400 mg; **Oral Tablet:** 300 mg, 600 mg, 800 mg; **Oral Solution:** 250 mg/5 mL; **Oral Tablet, Extended Release:** 300 mg, 600 mg



Teva generic 800 mg pictured

Glenmark generic 600 mg pictured



Northstar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Partial seizure, adjunct: Immediate release, Adults and Children ≥12 y of age, initial, 300 mg po tid, may titrate to 1800 mg/d in 3 divided doses (*max* 2400-3600 mg/d); Children 3-11 y of age, initial, 10-15 mg/kg/d in 3 divided doses, maintenance (Children 3-4 y of age), may titrate over 3 d to 40 mg/kg/d in 3 divided doses, maintenance (Children 5-11 y of age), may titrate over 3 d to 25-35 mg/kg/d in 3 divided doses.
2. Postherpetic neuralgia: Immediate release, Adults, 300 mg po on day 1, 300 mg bid on day 2, 300 mg tid on day 3, may titrate dose to 1800 mg/d in 3 divided doses; extended release, 300 mg on day 1, 600 mg on day 2, 900 mg days 3-6, 1200 mg days 7-10, 1500 mg days 11-14, and 1800 mg po daily thereafter

Off-Label Uses.

1. Diabetic peripheral neuropathy: Adults, 900-3600 mg/d po
2. Restless leg syndrome: 300 mg po 2 h prior to bedtime
3. Neuropathic pain: Immediate release, 300 mg po daily, may titrate to 3600 mg po daily

MOA. Gabapentin is a cyclohexane compound that is structurally related to GABA; its mechanism of action is not known. Gabapentin does not interact with GABA receptors or alter the formation, release, degradation, or reuptake of GABA.

Drug Characteristics: Gabapentin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 27-60%; food increases absorption
Dose Adjustment Renal	CrCl ≥60 mL/min, 900-3600 mg/d in 3 divided doses; CrCl 30-59 mL/min, 400-1400 mg/d in 2 divided doses; CrCl 15-29 mL/min, 200-700 mg/d given once daily	**Distribution**	Vd = 58 L; <3% protein bound
Dialyzable	Hemodialysis: 100-300 mg/d given once daily; give supplemental dose postdialysis	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 76-81% (unchanged) and 10-23% in feces, with a half-life of 5-7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Gabapentin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush or chew ER tablet	No	Motrin, Neoral, Nitrofurantoin, Noroxin	No

Drug Interactions: Gabapentin

Typical Agents	Mechanism	Clinical Management
Antacids	Decreased gabapentin absorption	Separate administration by 2 h

Adverse Reactions: Gabapentin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, somnolence	Ataxia, blurred vision, diarrhea, fatigue, hostile behavior, peripheral edema, nausea, nystagmus, vomiting, weight gain, xerostomia	Stevens-Johnson syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Reduction in seizure frequency or relief of pain associated with postherpetic neuralgia.

Toxicity Monitoring Parameters. Emergence or worsening of depression, suicidality, and/or any unusual behavioral or mood changes (anxiety, agitation, hostility, mania, and hypomania).

Key Patient Counseling Points. First dose on 1st day should be taken at bedtime. ER formulation should be taken with the evening meal. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness and somnolence. Report worsening depression, suicidal ideation, or unusual changes in behavior. Avoid sudden discontinuation of drug, as this may precipitate status epilepticus. Wait 2 h after antacid before taking gabapentin.

Clinical Pearls. Use in renally compromised patients <12 y of age has not been studied. Dosage interval should not exceed 12 h. Gabapentin dose reductions, discontinuation, or substitutions with alternative medications should be performed gradually over a min of 1 wk. Medication guide required at dispensing.

GATIFLOXACIN OPHTHALMIC: Zymar, Zymaxid

Class: Fluoroquinolone Antibiotic

Dosage Forms. **Ophthalmic Solution:** 0.5%

Common FDA Label Indication, Dosing, and Titration.

1. Bacterial conjunctivitis: Adults and Children ≥1 y of age, 0.5% ophthalmic solution, 1 drop to affected eye(s) q2h while awake × 2 days, then qid while awake for 5 more d

Off-Label Uses. None

MOA. Gatifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It is highly active against aerobic, gram-negative bacilli, especially Enterobacteriaceae. It has poor activity against streptococci and anaerobes.

Drug Characteristics: Gatifloxacin Ophthalmic

Dose Adjustment Hepatic	Not required	**Absorption**	After ocular instillation, serum concentrations are undetectable
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to gatif oxacin or other quinolones	**Black Box Warnings**	None

Allergan 0.3% solution pictured

Medication Safety Issues: Gatifloxacin Ophthalmic

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Gatifloxacin Ophthalmic. None known

Adverse Reactions: Gatifloxacin Ophthalmic

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Conjunctivitis, dry eyes, eye pain, subconjunctival hemorrhage, tearing and burning of the eyes, decreased visual acuity	Conjunctival hemorrhage

Efficacy Monitoring Parameters. Resolution of signs and symptoms of eye infection.

Toxicity Monitoring Parameters. Severe eye pain, itching, redness, or burning.

Key Patient Counseling Points. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Wash hands with soap and water before and after use. Lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye, but not touching, with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye.

Clinical Pearls. Bacterial conjunctivitis is very contagious and spread by direct contact.

GEMFIBROZIL: Lopid, Various

Class: Antihyperlipidemic

Dosage Forms. Oral Tablet: 600 mg

Teva generic 600 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Coronary arteriosclerosis; prophylaxis-familial combined hyperlipidemia: 600 mg po bid
2. Familial type V hyperlipoproteinemia-Fredrickson type IV hyperlipoproteinemia: 600 mg po bid

Off-Label Uses. None

MOA. Fibric acid derivatives activate PPARα, which increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). Activation of PPARα also induces an increase in the synthesis of apoproteins A-I and A-II and HDL-cholesterol.

Drug Characteristics: Gemfibrozil

Dose Adjustment Hepatic	Avoid in severe liver impairment	**Absorption**	Well absorbed, food reduces absorption, take on empty stomach
Dose Adjustment Renal	CrCl 10-50 mL/min, administer 75% of the dose; CrCl <10 mL/min, reduce dose by 50%	**Distribution**	Vd = 60 L; 99% protein bound
Dialyzable	Unknown	**Metabolism**	<20% hepatic, CYP3A4/5 substrate. Inhibitor of CYP1A2 (moderate), CYP2C19 (strong), CYP2C8 (strong), CYP2C9 (strong)
Pregnancy Category	C	**Elimination**	Renal elimination 70%, with a half-life of 2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to gemfibrozil, concurrent repaglinide or simvastatin, gallbladder disease, severe renal or hepatic dysfunction	**Black Box Warnings**	None

Medication Safety Issues: Gemfibrozil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Levbid, Lipitor, Lodine	No

Drug Interactions: Gemf brozil

Typical Agents	Mechanism	Clinical Management
Atorvastatin, HMG-CoA reductase inhibitors, colchicine, fibrates, niacin	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use, or monitor for myopathy and consider dose reductions
Cholestyramine, colestipol	Decreased absorption of gemfibrozil	Separate administration by 2 h
CYP1A2, CY2C19, CYP2C8, CYP2C9 substrates	Increased plasma concentrations of substrates via inhibition of CYPs by gemfibrozil	Avoid concurrent use if narrow therapeutic index, or monitor and consider dose reductions of substrate
CYP3A4/5 inhibitors	Decreased metabolism of gemfibrozil increases risk of gemfibrozil toxicity	Monitor for toxicity and consider dose reductions of gemfibrozil
CYP3A4/5 inducers	Increased metabolism of gemfibrozil reduces gemfibrozil efficacy	Monitor for efficacy and consider dose increases of gemfibrozil
Glyburide	Increased risk of hypoglycemia via competition for renal tubular secretion	Avoid concurrent use

Adverse Reactions: Gemf brozil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Indigestion	Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea, rash	Rhabdomyolysis, cholelithiasis, hepatotoxicity, mood disorder, impotence, agranulocytosis

Efficacy Monitoring Parameters. Primary, reduction in triglyceride levels. Secondary, reduction in total cholesterol, LDL-cholesterol, increase in HDL-cholesterol levels. Monitor baseline and every 6 mo.

Toxicity Monitoring Parameters. Seek medical attention if signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, and severe abdominal pain. LFTs and complete blood counts should be performed at baseline, 12 wk after initiation of therapy or dose increases. Serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

Key Patient Counseling Points. Take 30 min before breakfast and dinner. Instruct patient to report signs/symptoms of rhabdomyolysis, jaundice (yellowing of skin or eyes), or renal failure.

Clinical Pearls. The fibric acid derivatives (gemfibrozil, clofibrate, and fenofibrate) are recommended as alternatives to niacin in the treatment of types IIb, III, IV, and V hyperlipidemia.

GLIMEPIRIDE: Amaryl, Various

Class: Second-Generation Sulfonylurea, Antidiabetic

Dosage Forms. Oral Tablet: 1 mg, 2 mg, 4 mg

Common FDA Label Indication, Dosing, and Titration.

Diabetes mellitus, type 2: 1-2 mg po daily, may titrate by 1-2 mg every 1-2 wk to effect, *max* dose 8 mg po daily

Off-Label Uses. None

MOA. Sulfonylureas enhance insulin secretion from pancreatic β-cells and potentiate insulin action on several extrahepatic tissues. Long-term sulfonylureas increase peripheral utilization of glucose, suppress hepatic gluconeogenesis, and possibly increase the sensitivity and/or number of peripheral insulin receptors.

2 mg 4 mg

Teva generic pictured

Drug Characteristics: Glimepiride

Dose Adjustment Hepatic	Avoid use in patients with severe liver dysfunction	**Absorption**	F = 100%, food decreases absorption
Dose Adjustment Renal	Start with 1 mg po daily	**Distribution**	Vd = 8.8 L; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic, CYP2C9 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 60% with a half-life of 5-9 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	G6PD
Contraindications	Hypersensitivity to sulfonylureas, diabetic ketoacidosis	**Black Box Warnings**	None

Medication Safety Issues: Glimepiride

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	GlipiZIDE	No

Drug Interactions: Glimepiride

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia. Symptoms of hypoglycemia masked	Avoid propranol; use others with caution and increased monitoring
CYP2C9 inducers	Increased glimepiride metabolism and decreased glimepiride efficacy	Monitor blood glucose and consider dose increases of sulfonylureas
CYP2C9 inhibitors	Decreased glimepiride metabolism and increased risk of glimepiride toxicity	Monitor blood glucose and consider dose decreases of sulfonylureas
Fluoroquinolones, NSAIDs, fenofibrate, SSRIs, somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Sulfonamides	Increased risk of hypoglycemia	Monitor blood glucose and consider dose adjustments of sulfonylureas

Adverse Reactions: Glimepiride

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Hypoglycemia, nausea, headache, dizziness, asthenia	Cutaneous hypersensitivity, hemolytic anemia, hepatotoxicity, disulfiram reaction

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness. Seek medical attention if yellowing of skin or eyes, severe skin rash, unusual bruising, or bleeding.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Take with food or milk in the morning. Use a sunscreen and avoid sunlamps and tanning beds. Do not drink alcohol; may cause a disulfiram reaction.

Clinical Pearls. Metformin is first-line therapy for type 2 diabetes. A sulfonylurea may be added if HbA_{1c} goals are not achieved with metformin alone. Not for use in children. Hemolytic anemia is most likely to occur in patients with G6PD deficiency.

GLIPIZIDE: Glucotrol, Various

Class: Second-Generation Sulfonylurea, Antidiabetic

Dosage Forms. Oral Tablet: 5 mg, 10 mg; **Oral Tablet, Extended Release:** 2.5 mg, 5 mg, 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus: Immediate release, 5-10 mg po daily, may titrate to *max* of 40 mg daily, divide bid if doses >15 mg; extended release, 5-10 mg po daily, may titrate to *max* of 20 mg daily

Off-Label Uses. None

MOA. Sulfonylureas enhance insulin secretion from pancreatic β-cells and potentiate insulin action on several extrahepatic tissues. Long-term sulfonylureas increase peripheral utilization of glucose, suppress hepatic gluconeogenesis, and possibly increase the sensitivity and/or number of peripheral insulin receptors.

Sandoz generic
5 mg pictured

Watson generic
5 mg ER pictured

Greenstone generic
2.5 mg ER pictured

Sandoz generic
10 mg pictured

Watson generic
10 mg ER pictured

Greenstone generic
5 mg ER pictured

Drug Characteristics: Glipizide

Dose Adjustment Hepatic	Start with 2.5 mg po daily	**Absorption**	Immediate release and extended release: F = 100%, food delays absorption by 40 min
Dose Adjustment Renal	Start with 2.5 mg po daily	**Distribution**	Vd = 11 L; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	80% hepatic, CYP2C9 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 2-5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	G6PD
Contraindications	Hypersensitivity to sulfonylureas, diabetic ketoacidosis, type 1 diabetes	**Black Box Warnings**	None

Medication Safety Issues: Glipizide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	GlipiZIDE	Do not crush XL form	Yes	Glimepiride, glyBURIDE	No

Drug Interactions: Glipizide

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia. Symptoms of hypoglycemia masked	Avoid propranol; use others with caution and increased monitoring
CYP2C9 inducers	Increased glipizide metabolism and decreased glipizide efficacy	Monitor blood glucose and consider dose increases of sulfonylureas
CYP2C9 inhibitors	Decreased glipizide metabolism and increased risk of glipizide toxicity	Monitor blood glucose and consider dose decreases of sulfonylureas
Fluoroquinolones, NSAIDs, fenofibrate, SSRIs, somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, glycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Sulfonamides	Increased risk of hypoglycemia	Monitor blood glucose and consider dose adjustments of sulfonylureas

Adverse Reactions: Glipizide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Asthenia	Hypoglycemia, nausea, headache, tremors, constipation, diarrhea, dizziness, nervousness, tremor	Cutaneous hypersensitivity, hemolytic anemia, hepatotoxicity, disulfiram reaction

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness. Seek medical attention if yellowing of skin or eyes, severe skin rash, unusual bruising, or bleeding.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Use a sunscreen and avoid sunlamps and tanning beds. Do not drink alcohol; may cause a disulfiram reaction. Take 30 min before morning meal. Do not chew or crush extended-release formulation.

Clinical Pearls. Metformin is first-line therapy for type 2 diabetes. A sulfonylurea may be added if HbA_{1c} goals are not achieved with metformin alone. Not for use in children. Hemolytic anemia is most likely to occur in patients with G6PD deficiency. Patients on insulin: when starting glipizide, reduce insulin dose by 50%, or discontinue if <20 units/d.

HAEMOPHILUS INFLUENZAE, TYPE B, CONJUGATE: Hiberix, PedvaxHIB, ActHIB

Class: Vaccine

Dosage Forms. **Lyophilized Powder for Intramuscular Injection:** 0.5 mL after reconstitution; also available in combination with other pediatric vaccines

Common FDA Label Indication, Dosing, and Titration.

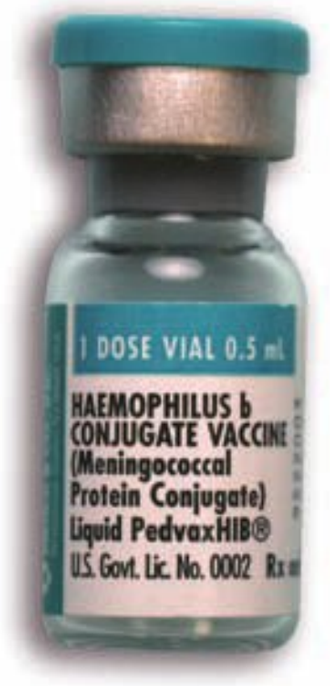
1. Prevention of invasive *H. influenzae* type B infection, Children: Dose schedule depends on product and timing of start of vaccination series. For ActHIB, dose at 2, 4, 6, and 12-15 mo of age as primary series. If PedvaxHIB used, doses at 2, 4, and 12-15 mo are used. If dosing begins later than 2 mo, adjusted dosing schedule used and number of doses changes. Hiberix can be used only for the last dose for children aged 12 mo to 4 y.

Off-Label Uses.

1. Prevention of invasive *H. influenzae* type B infection, Adults: 1 dose. May use any of the Hib conjugate vaccines for unvaccinated or partially vaccinated persons aged ≥5 y who have leukemia, malignant neoplasms, anatomic or functional asplenia (including sickle cell disease), HIV infection, or other immunocompromising conditions.

Drug Characteristics: H. influenzae **Type B, Conjugate**

Pregnancy Category	C	**ADME**	None known
Lactation	Unlikely to be used in lactating woman; vaccines generally considered safe during lactation	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to Hib vaccine or a component of the vaccine	**Black Box Warnings**	None



Merck pictured

Medication Safety Issues: H. influenzae **Type B, Conjugate**

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	None	No

Drug Interactions: H. influenzae **Type B, Conjugate**

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression	Delay Hib vaccine administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents	Immunosuppression	Delay Hib vaccine administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: H. influenzae **Type B, Conjugate**

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence	Fever, nausea, malaise	Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of invasive *H. influenzae* type B infection.

Toxicity Monitoring Parameters. Monitor for syncope for 15 min after administration. Monitor for fever following administration.

Key Patient Counseling Points. Return to provider for each dose in the series.

Clinical Pearls. Clinicians can exchange among brands of vaccines for the primary series (with the exception of Hiberix). Seroconversion after 1 dose is 75-90%. Onset of action is 1-2 wk and immunity lasts 1.5 y.

HEPATITIS A VACCINE, INACTIVATED: Havrix, Vaqta

Class: Vaccine

Dosage Forms. **Intramuscular Suspension:** Havrix, 720 ELISA units/0.5 mL, 1440 ELISA units/mL; Vaqta 25 units/0.5 mL, 50 units/1 mL; also available in combination with hepatitis B vaccine

Common FDA Label Indication, Dosing, and Titration.

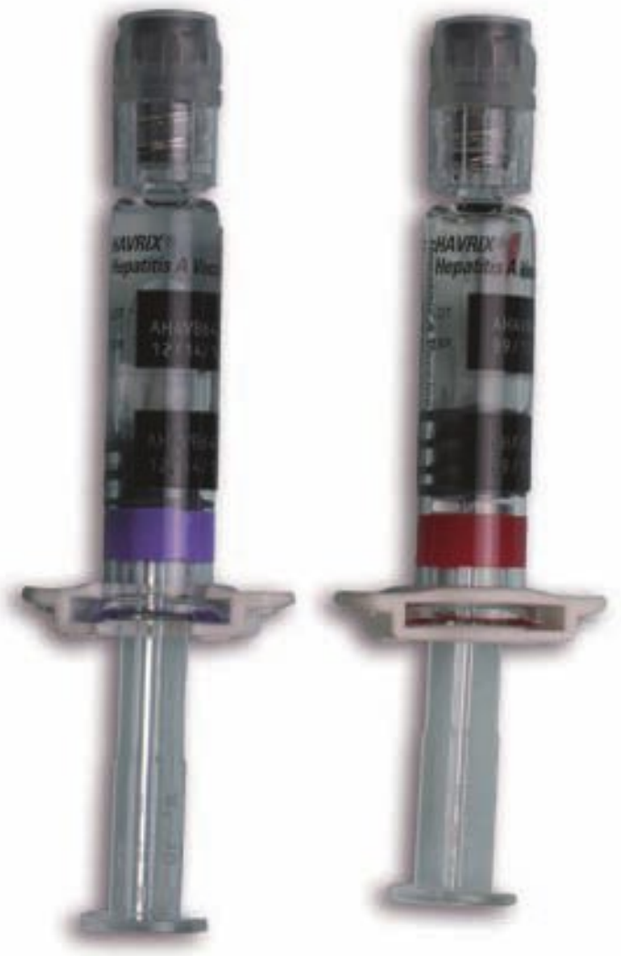
1. Hepatitis A prophylaxis: Adults, Havrix 1440 ELISA units IM once, with a 2nd dose 6-12 mo later, or Vaqta 50 units IM once, with a 2nd dose 6-18 mo later; Children 12 mo to 18 y, Havrix 720 ELISA units IM once, with a 2nd dose 6-12 mo later, or Vaqta 25 units IM once, with a booster dose 6-18 mo later

Off-Label Uses.

1. Hepatitis A postexposure prophylaxis for individuals aged 1-40 y: Same regimen as for preexposure prophylaxis; vaccine series should be started within 2 wk of exposure

Drug Characteristics: Hepatitis A Vaccine, Inactivated

Pregnancy Category	C	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hepatitis A vaccine or a component of the vaccine	**Black Box Warnings**	None



GlaxoSmithKline pictured

Medication Safety Issues: Hepatitis A Vaccine, Inactivated

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	None	No

Drug Interactions: Hepatitis A Vaccine, Inactivated

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression	Delay hepatitis A vaccine administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents	Immunosuppression	Delay hepatitis A vaccine administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: Hepatitis A Vaccine, Inactivated

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence	Fever, nausea, malaise	Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of hepatitis A infection; although antibody concentrations might be measured, routine measurement for vaccine response is not recommended.

Toxicity Monitoring Parameters. Monitor for syncope, fever, or anaphylactic hypersensitivity reaction after administration. LFTs for adults at risk for liver failure.

Key Patient Counseling Points. Return to provider for booster dose in 6-12 mo or 6-18 mo after 1st dose (depending on product initially used).

Clinical Pearls. Not indicated for children <12 mo of age. The vaccines are interchangeable, so 2nd dose can be administered with the other brand of vaccine. Administer 2 wk prior to exposure (travel or international adoption of child). Vaccination recommended for all children ≥12 mo of age, and adults at risk for hepatitis A infection, including homosexual men, IV drug users, patients with chronic liver disease, international travelers, and those in close contact with those from endemic areas (Africa, India, etc). Hepatitis A transmits via oral/fecal route. After vaccination, 94-100% seroconversion within 1 mo.

HEPATITIS B VACCINE, RECOMBINANT: Engerix-B, Recombivax HB

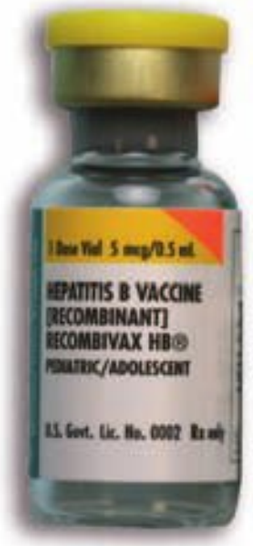
Class: Vaccine

Dosage Forms. **Suspension for Intramuscular Injection:** Engerix 10 mcg/0.5 mL, 20 mcg/1 mL; Recombivax 5 mcg/0.5 mL, 10 mcg/1 mL, 40 mcg/1 mL; also available in combination with hepatitis A vaccine and in combination products with other pediatric vaccines

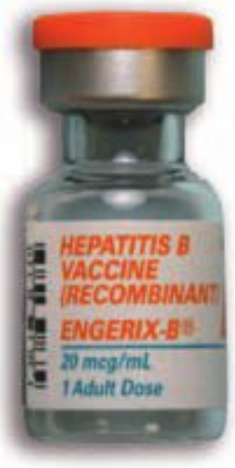
Common FDA Label Indication, Dosing, and Titration.

1. Prevention of hepatitis B infection: Adults ≥20 y of age, Engerix 20 mcg IM or Recombivax 10 mcg IM given once, with 2 additional doses given 1 and 5 mo later; Children, Engerix 10 mcg IM or Recombivax 5 mcg IM given once, with 2 additional doses given 1 and 5 mo later; Patients undergoing hemodialysis, 40 mcg IM given once, with 2 additional doses given 1 and 5 mo later; several alternative regimens approved for adults and children of varying ages

Off-Label Uses. None



GlaxoSmithKline pictured



Merck pictured

Drug Characteristics: Hepatitis B Vaccine, Recombinant

Pregnancy Category	C	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	Not clinically relevant
Contraindications	Hypersensitivity to hepatitis B vaccine or a component of the vaccine, including yeast	**Black Box Warnings**	None

Medication Safety Issues: Hepatitis B Vaccine, Recombinant

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Engerix-B, Recombivax HB	No	No	No	Adult and pediatric formulations of Engerix-B	No

Drug Interactions: **Hepatitis B Vaccine, Recombinant.** None

Adverse Reactions: Hepatitis B Vaccine, Recombinant

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness	Fever	Anaphylaxis, pancytopenia

Efficacy Monitoring Parameters. Prevention of hepatitis B infection; measurement of antibody to the surface antigen (anti-HBs) 1-2 mo after dose 3 is recommended for individuals at risk for vaccine nonresponse and is required for those at occupational risk for hepatitis B exposure.

Toxicity Monitoring Parameters. Monitor for syncope, fever, seizure-like activity, or anaphylactic hypersensitivity reaction after administration.

Key Patient Counseling Points. Return to provider for all doses in the series.

Clinical Pearls. The brands of vaccines are considered interchangeable for the series. Use a needle of appropriate length to ensure intramuscular administration. Recommended for all infants, adolescents, health-care personnel, patients with renal failure, individuals with hepatitis C, residents and staff of psychiatric institutions, household and contacts of individuals with chronic hepatitis B, those with frequent exposure to blood products, international travelers, those at increased risk due to sexual practices, prisoners, and injection drug users. Lifetime immunity achieved in those with initial response.

HUMAN PAPILLOMAVIRUS VACCINE: Cervarix, Gardasil

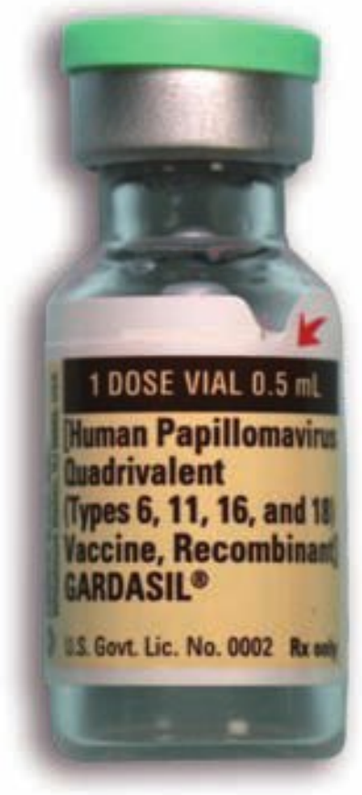
Class: Vaccine

Dosage Forms. **Intramuscular Suspension**: Cervarix HPV (bivalent) 16 L1 protein 20 mcg/0.5 mL and HPV 18 L1 protein 20 mcg/0.5 mL; Gardasil HPV (quadrivalent) 6 L1 protein 20 mcg/0.5 mL, HPV 11 L1 protein 40 mcg/0.5 mL, HPV 16 L1 protein 40 mcg/0.5 mL, and HPV 18 L1 protein 20 mcg/0.5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Human papillomavirus bivalent vaccine (HPV2, Cervarix, types 16 and 18): Prevention of cervical cancer and precancerous lesions in females aged 10-25 y, 3 dose series at 0, 1, and 6 mo
2. Human papillomavirus quadrivalent vaccine (HPV4, Gardasil, types 6, 11, 16, and 18): Prevention of cancer and precancerous lesions of the cervix, vulva, vagina, and anus and genital warts in individuals aged 9-26 y, 3 dose series at 0, 2, and 6 mo
3. Routine immunization of females is recommended at age 11-12 y with either vaccine preparation. Catch-up immunization is recommended for females aged 13-26 y
4. Routine immunization of males is recommended at age 11-12 y with HPV4 (Gardasil). Catch-up immunization is recommended for males aged 13-21 y. HPV4 (Gardasil) is recommended for men who have sex with men aged 22-26 y

Off-Label Uses. None



Merck pictured

Drug Characteristics: Human Papillomavirus Vaccine

Pregnancy Category	B; recommend completing the series after pregnancy completion	**ADME**	None known
Lactation	Caution advised; weigh risk and benefit	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to HPV vaccine or a component of the vaccine; Cervarix, yeast allergy; Gardasil, latex allergy	**Black Box Warnings**	None

Medication Safety Issues: Human Papillomavirus Vaccine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Bivalent and quadrivalent products often confused	No

Drug Interactions: Human Papillomavirus Vaccine

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression	Delay vaccine administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents	Immunosuppression	Delay vaccine administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: Human Papillomavirus Vaccine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Arthralgia, myalgia, headache, fever	Rash, GI symptoms	Anaphylaxis, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of cervical cancer, other diseases caused by HPV.

Toxicity Monitoring Parameters. Syncope; continue routine cervical cancer screening; negative HPV test not required for vaccination.

Key Patient Counseling Points. Return to provider for all doses in the series.

Clinical Pearls. Complete the vaccine series with the same brand whenever possible. Syncope is common following vaccine administration. Observe immunized individual for 15 min following vaccine administration. Individuals already infected with HPV will not be protected by vaccine. Does not treat active HPV infection or other subtypes of HPV not included in vaccine. HPV types 16 and 18 cause 70% of cervical cancers; Cervarix only protects against cervical cancer. HPV types 6 and 11 cause 90% of genital warts; Gardasil protects against both cervical cancer and genital warts.

HYDRALAZINE: Apresoline, Various

Barr generic pictured

Par generic
10 mg pictured

Class: Peripheral Vasodilator

Dosage Forms. **Oral Tablet:** 10 mg, 25 mg, 50 mg, 100 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, initial, 10 mg po qid for 2-4 d, may titrate to 25 mg po qid for 3-5 d, then titrate to lowest effective dose at intervals of 1 wk (*max* 300 mg/d); Children, 0.75-1 mg/kg/d po in 2-4 divided doses; may titrate dose gradually over 3-4 wk (*max* dose 7.5 mg/kg or 200 mg/d)

Off-Label Uses.

1. Heart failure: Adults, 25-50 mg po daily in 3-4 divided doses in combination with isosorbide dinitrate (*max* hydralazine dose of 300 mg/d in divided doses)

MOA. Hydralazine is a vasodilator that reduces total peripheral resistance by direct action on vascular smooth muscle, with an effect greater on arterioles than on veins.

Drug Characteristics: Hydralazine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 38-50%, no effect of food on absorption
Dose Adjustment Renal	CrCl 10-50 mL/min, increase dosing interval to q8h; CrCl <10 mL/min, increase dosing interval to q8-16h	**Distribution**	88-90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism to 2 metabolites not via CYP
Pregnancy Category	C	**Elimination**	Renal elimination is 3-14% and 3-12% in feces, with a half-life of 3-5 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hydralazine; dissecting aortic aneurysm	**Black Box Warnings**	None

Medication Safety Issues: Hydralazine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	HydrALAZINE	No	No	HydrOXYzine	No

Drug Interactions: Hydralazine

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of hydralazine	Avoid concurrent use or monitor BP
Furosemide	Increased diuretic response to furosemide	Monitor serum electrolytes, diuresis, CrCl
Metoprolol, propranolol	Increased beta-blocker toxicity (bradycardia, fatigue, shortness of breath)	If concurrent therapy required, take with food or switch to sustained-release beta-blocker; monitor BP

Adverse Reactions: Hydralazine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Anorexia, chest pain, diarrhea, dizziness, headache, hypotension, nasal congestion, palpitations, reflex tachycardia, vomiting	Agranulocytosis, hepatotoxicity, leucopenia, systemic lupus erythematosus

Efficacy Monitoring Parameters. Decrease in systolic and diastolic BP, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of hypotension or liver damage. CBC and antinuclear antibody titers at baseline and periodically during prolonged treatment.

Key Patient Counseling Points. Patient should not drink alcohol while taking drug. Advise patient against sudden discontinuation of drug as this may cause rebound hypertension. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Patient should report chest pain, palpitations, signs/symptoms of tachyarrhythmia, hypotension, agranulocytosis, systemic lupus erythematosus, or hepatotoxicity.

Clinical Pearls. Hydralazine is not a first-line therapy for hypertension. Hydralazine may cause drug-induced lupus erythematosus (DILE), and has a higher incidence compared to other drugs associated with DILE. Thiazide diuretics, calcium channel blockers, ACE-Is, and ARBs are preferred. Hydralazine may be beneficial in patients intolerant of ACE-Is or ARBs and when added ACE-Is or ARBs in African Americans.

HYDROCHLOROTHIAZIDE: Esidrix, Various

Class: Thiazide Diuretic, Antihypertensive

Dosage Forms. **Oral Capsule:** 12.5 mg; **Oral Tablet:** 12.5 mg, 25 mg, 50 mg

Teva generic pictured

Watson generic 12.5 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Edema; adjunct: Adults, 25-100 mg po daily in single or divided doses; Children, 1-2 mg/kg po daily in single or divided doses; Infants <6 mo of age may require doses up to 3 mg/kg po daily in 2 divided doses; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d
2. Hypertension: Adult, initial, 12.5-25 mg po daily, may titrate to 50-100 mg po daily in single or divided doses; Children, 1-2 mg/kg po daily in single or divided doses; Infants <6 mo of age may require doses up to 3 mg/kg po daily in 2 divided doses, *max* dose 37.5 mg/d; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d

Off-Label Uses.

1. Hypercalciuria: Adults, 25 mg po bid; Children, 1-2 mg/kg/d po

MOA. Thiazides increase sodium and chloride excretion by interfering with their reabsorption in the cortical diluting segment of the nephron.

Drug Characteristics: Hydrochlorothiazide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60-80%, reduced in patients with hepatic, renal, or cardiac (heart failure) disease
Dose Adjustment Renal	CrCl <25 mL/min, avoid	**Distribution**	Vd = 3.6-7.8 L/kg; 40% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	Eliminated 50-70% unchanged in urine, half-life 10-12 h (prolonged in patients with heart failure or renal disease)
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hydrochlorothiazide or sulfonamide, concomitant dofetilide therapy, or anuric patients	**Black Box Warnings**	None

Medication Safety Issues: Hydrochlorothiazide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	HCTZ is an error-prone abbreviation Maxide, Micronase	No

Drug Interactions: Hydrochlorothiazide

Typical Agents	Mechanism	Clinical Management
ACE-Is	Increased risk of postural hypotension (1st dose)	Start with low dose of ACE-I and monitor BP
Antiarrhythmic agents, digoxin	Increased risk of ventricular arrhythmias (torsades de pointes) due to hypokalemia, hypomagnesemia	Monitor serum potassium and magnesium levels; supplement electrolyte if necessary
Antidiabetic medications	Decreased hypoglycemic effect	Monitor blood glucose levels
Calcium supplements	Increased risk of hypercalcemia	Avoid concurrent use or monitor serum calcium levels
Carbamazepine	Increased risk of hyponatremia	Avoid concurrent use or monitor serum sodium levels
NSAIDs	Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and serum creatinine levels
Topiramate, lithium	Increased topiramate or lithium concentrations and increased risk of toxicity	Monitor levels and consider dose reduction

Adverse Reactions: Hydrochlorothiazide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypotension, dizziness, headache	Constipation, hypercalcemia, hyperglycemia, hyperuricemia, hypokalemia, hypomagnesemia, hyponatremia, impotence, loss of appetite, nausea, photosensitivity, rash	Cardiac arrhythmias, hepatitis, pancreatitis, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Decreased BP, reductions in edema.

Toxicity Monitoring Parameters. Decreased serum and urine electrolytes, decreased renal function, increased serum uric acid or blood glucose. Seek medical attention if skin rash, yellowing of eyes or skin, decreased urine output, or symptoms of gout occur.

Key Patient Counseling Points. May be taken with or without food. Take early in the day to avoid nocturia. May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Report signs/symptoms of hypotension. Eat high-potassium foods during therapy. Avoid alcohol and using NSAIDs.

Clinical Pearls. Full hypotensive effect may require 2-3 wk. Thiazides are first-line therapies for managing hypertension. Available as a component of many combination products with other antihypertensives.

HYDROCODONE: Zohydro ER, Vicodin, Various

5 mg/325 mg | 7.5 mg/325 mg | 10 mg/325 mg | 10 mg/500 mg | 7.5 mg/500 mg

Mallinckrodt generic pictured

Class: Opioid Analgesic. C-II

Dosage Forms. **Oral Capsule, Extended Release (Hydrocodone Alone):** 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg; **Oral Tablet (With Acetaminophen):** Hydrocodone/Acetaminophen 2.5 mg/325 mg, Hydrocodone/Acetaminophen 5 mg/325 mg, Hydrocodone/Acetaminophen 7.5 mg/325 mg, Hydrocodone/Acetaminophen 10 mg/325 mg; **Oral Elixir, Oral Solution (With Acetaminophen):** Hydrocodone/Acetaminophen 7.5 mg/325 mg per 15 mL, Hydrocodone/Acetaminophen 10 mg/325 mg per 15 mL

Common FDA Label Indication, Dosing, and Titration.

1. Pain, moderate to moderately severe: Adults: 10 mg q 12 h initially, may titrate to response

Off-Label Uses. None

MOA. Hydrocodone is an opioid analgesic and antitussive with unknown mechanism of action, but it is thought to be related to the presence of opiate receptors in the CNS.

Drug Characteristics: Hydrocodone

Dose Adjustment Hepatic	Severe: Start with 10mg dose	**Absorption**	Well absorbed, minimal food effect
Dose Adjustment Renal	Severe: Start with 10mg dose	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Pro-drug activated to hydromorphone by CYP2D6, deactivated by CYP3A4/5
Pregnancy Category	C	**Elimination**	26% renal, half-life of 8 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, paralytic ileus, respiratory depression, severe asthma	**Black Box Warnings**	Addiction potential, respiratory depression, accidental exposure, neonatal opioid withdrawal, alcohol, CYP3A4/5 interactions

Medication Safety Issues: Hydrocodone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ER	HYDROcodone	Do not chew or crush ER formulation	Yes	HYDROmorphone, oxyCODONE	No

Drug Interactions: Hydrocodone

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Buprenorphine, opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP3A4/5 inducers	Increased hydrocodone metabolism decreases hydrocodone efficacy	Monitor and consider hydrocodone dose increase
CYP3A4/5 inhibitors	Decreased hydrocodone metabolism and increased hydrocodone toxicity	Avoid concurrent strong CYP3A4/5 inhibitors, uses moderate CYP3A4/5 inhibitors with caution and consider a hydrocodone dose decrease
CYP2D6 inhibitors	Decreased activation of hydrocodone to hydromorphone, decreased hydrocodone efficacy	Monitor and consider dose increases of hydrocodone
MAOIs	Additive respiratory depression	Avoid concurrent use

Adverse Reactions: Hydrocodone/Acetaminophen

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, GI distress, somnolence	Rash, respiratory depression, euphoria, pruritus	Stevens-Johnson syndrome, physical dependence, tolerance, respiratory depression

Efficacy Monitoring Parameters. Relief of pain.

Toxicity Monitoring Parameters. Seek medical attention if severe skin rash, excessive drowsiness, decreased breathing, severe constipation, black tarry stools, or yellowing of eyes or skin.

Key Patient Counseling Points. Use a stool softener and/or laxative for preventing constipation with chronic use. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

Clinical Pearls. Use caution in elderly, appear more sensitive to the effect. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. If using a combination product including acetaminophen, do not exceed *max* daily dose (4 g) of acetaminophen. The *max* dose of acetaminophen in combination products is 325 mg per dosage unit as of April 2014; higher strengths were common and are in the process of being withdrawn from the market. All hydrocodone-containing combination products are now schedule II, including Vicodin. Various other combinations available, including hydrocodone with chlorpheniramine cough liquid (Tussionex).

HYDROCORTISONE TOPICAL: Various

2.5% cream

1% cream

Fougera generic pictured

Class: Topical Corticosteroid

Dosage Forms. **Rectal Cream:** 1%, 2.5%; **Topical Cream:** 0.5%, 1%, 2.5%; **Topical Lotion:** 1%, 2.5%; **Topical Ointment:** 0.5%, 1%, 2.5%

H

Common FDA Label Indication, Dosing, and Titration.

1. Skin disorders, corticosteroid responsive: Apply thin layer topically to affected area daily to bid

Off-Label Uses. None

MOA. Hydrocortisone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Drug Characteristics: Hydrocortisone Topical

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption unless covering large surface area or covering areas lacking skin integrity
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed

Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hydrocorti-sone or other corticosteroids	**Black Box Warnings**	None

Medication Safety Issues: Hydrocortisone Topical

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
HC, Maximum strength	No	No	No	HCT (occasional abbreviation for hydrocortisone) is an error-prone abbreviation, may be confused with HCTZ (hydrochlorothiazide)	No

Drug Interactions: **Hydrocortisone Topical.** None known

Adverse Reactions: Hydrocortisone Topical

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dry skin, burning sensation, stinging, pruritus at site of administration; headache	HPA suppression has been reported when used with occlusive dressings, or when applied over larger surface areas

Efficacy Monitoring Parameters. Improvement in clinical signs of skin disorder.

Toxicity Monitoring Parameters. Seek medical attention if severe skin irritation or symptoms worsen after administration.

Key Patient Counseling Points. Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration. Wash hands after application.

Clinical Pearls. Large number of dosage presentations (foams, gels, shampoos, etc), both by prescription and over the counter, are available. Oral and rectal formulations, administered for systemic action, also available and used for similar indications as other oral corticosteroids (eg, prednisone). Application to large surface areas, prolonged use, and occlusive dressings may increase risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption.

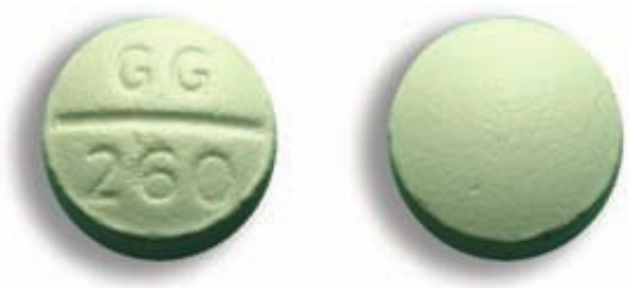
HYDROXYCHLOROQUINE: Plaquenil, Various

Class: Aminoquinoline

Dosage Forms. Oral Tablet: 200 mg

Common FDA Label Indication, Dosing, and Titration.

1. Lupus erythematosus: 400-800 mg po daily (may divide into 2 doses), then may reduce to maintenance dose of 200-400 mg po daily
2. Malaria, suppression: Adults, 400 mg po q week on the same day; Children, 5 mg base/kg (200 mg hydroxychloroquine sulfate = 155 mg hydroxychloroquine base); begin 2 wk prior to entering an endemic area and continue for 4 wk after leaving the endemic area
3. Rheumatoid arthritis: maintenance: 400-600 mg po daily, after 4-12 wk reduce dose to 200-400 mg for maintenance therapy



Goldline generic 200 mg pictured

Off-Label Uses. None

MOA. The mechanism of action of hydroxychloroquine is unknown. It is effective in treating *P. vivax, P. malariae*, and susceptible strains of *P. falciparum*.

Drug Characteristics: Hydroxychloroquine

Dose Adjustment Hepatic	Severe hepatic dysfunction, avoid	**Absorption**	F = 74%, minimal food effect
Dose Adjustment Renal	Severe renal dysfunction, avoid	**Distribution**	Concentration in red blood cells is 5 times higher than plasma
Dialyzable	Not dialyzable	**Metabolism**	40% and occurs by unknown enzymes
Pregnancy Category	D	**Elimination**	Renal elimination 16-25%, with a half-life of 40 d
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hydroxychloroquine, retinal or visual field changes from prior hydroxychloroquine, long-term use in children	**Black Box Warnings**	Experienced physician

Medication Safety Issues: Hydroxychloroquine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Platinol	No

Drug Interactions: Hydroxychloroquine

Typical Agents	Mechanism	Clinical Management
Aurothioglucose	Increased risk of blood dyscrasias	Contraindicated
Digoxin	Increased digoxin levels	Avoid concurrent use or monitor digoxin levels
Fibrates	Increased risk of cholelithiasis	Avoid concurrent use or monitor for cholelithiasis
Metoprolol	Decreased metabolism and increased toxicity of metoprolol	Avoid concurrent use

Adverse Reactions: Hydroxychloroquine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, constipation, diarrhea, headache, nausea, dizziness, visual disturbances, hyperpigmentation	Arrhythmias, cardiomyopathy, Stevens-Johnson syndrome, agranulocytosis, seizures, retinopathy, psychosis

Efficacy Monitoring Parameters. Rheumatoid arthritis: decreased pain and improved range of motion. Lupus: decreased joint pain, decrease in butterfly rash, improved energy.

Toxicity Monitoring Parameters. Seek medical attention if heart palpitations, severe rash, unusual bruising or bleeding, or difficulty seeing or changes in visual fields. Baseline and periodic eye exams.

Key Patient Counseling Points. If taking weekly, take on same day each week. Take with food or milk.

Clinical Pearls. One tablet of 200 mg of hydroxychloroquine sulfate is equivalent to 155 mg base. If serious adverse effects or overdose occurs, ammonium chloride (8 g daily in divided doses for adults) may be administered 3-4 d a week for several months to increase the renal excretion of hydroxychloroquine.

HYDROXYZINE: Atarax, Vistaril, Various

Class: Antihistamine

Dosage Forms. **Oral Tablet:** 10 mg, 25 mg, 50 mg; **Oral Capsule:** 25 mg, 50 mg, 100 mg; **Oral Syrup:** 10 mg/5 mL; **Oral Solution:** 10 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Anxiety: 50-100 mg po qid
2. Pruritus: 25 mg po tid-qid
3. Sedation: 50-100 mg po q4h prn

Off-Label Uses.

1. Seasonal allergic rhinitis: 10-25 mg po tid-qid

Northstar Rx generic pictured

MOA. Hydroxyzine hydrochloride is a rapid-acting agent with probable action of suppressing activity in key locations of the CNS's subcortical area. Primary skeletal muscle relaxation, bronchodilator activity, antiemetic effects, and antihistaminic and analgesic effects have been demonstrated experimentally and confirmed clinically.

Drug Characteristics: Hydroxyzine

Dose Adjustment Hepatic	Patients with chronic liver failure receive a lower dose; administer lowest effective dose once daily only and increase carefully to avoid toxicity	**Absorption**	Rapidly absorbed after oral administration
Dose Adjustment Renal	Not required	**Distribution**	Vd = 16 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Metabolized to cetirizine in the liver
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 3-20 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cetirizine or hydroxyzine	**Black Box Warnings**	None

Medication Safety Issues: Hydroxyzine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	HydrOXYzine	No	No	HydrALAZINE, hydroxyurea	Avoid. Highly anticholinergic.

Drug Interactions: Hydroxyzine

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Possible increase in sedation effects	Use concurrently with caution

Drug Interactions: Hydroxyzine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Sedation, headache, dry mouth, fatigue	

Efficacy Monitoring Parameters. Improvement in symptoms for which administered (anxiety, pruritus, insomnia).

Toxicity Monitoring Parameters. Seek medical attention for signs of severe CNS toxicity.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

Clinical Pearls. Product is available OTC in several dosage forms. Injectable formulation available for use as an adjunct to pain medications and antiemetics for perioperative pain, nausea, and vomiting, and alone as a sedative.

IBANDRONATE: Boniva, Various

Class: Bisphosphonate

Dosage Forms. Oral Tablet: 150 mg

Common FDA Label Indication, Dosing, and Titration.

1. Postmenopausal osteoporosis (Treatment): 150 mg po once monthly
2. Postmenopausal osteoporosis (Prophylaxis): 150 mg po once monthly

Off-Label Uses. None

MOA. Ibandronate binds to bone hydroxyapatite and, at the cellular level, inhibits osteoclast activity, thereby modulating bone metabolism.

Drug Characteristics: Ibandronate

Dose Adjustment Hepatic	Not required	**Absorption**	F <1%, food impairs absorption; take 30-60 min prior to meal
Dose Adjustment Renal	CrCl <30 mL/min, avoid use	**Distribution**	Vd = 90 L; 85-99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	50% renal elimination with a half-life of 37-157 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Esophageal abnormalities, which delay esophageal emptying, hypocalcemia, inability to sit or stand upright for at least 60 min	**Black Box Warnings**	None

GlaxoSmithKline 150 mg pictured

Medication Safety Issues: Ibandronate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew, crush, or suck tablet	No	No	No

Drug Interactions: Ibandronate

Typical Agents	Mechanism	Clinical Management
Aluminum, calcium-containing products	Decreased bisphosphonate absorption	Separate administration by 1-2 h
H_2-blockers and PPIs	Decreased bisphosphonate absorption	Separate administration by 1-2 h

Adverse Reactions: Ibandronate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Indigestion, backache, respiratory tract infections	Hypertension, diarrhea, abdominal pain, headache, myalgia	Osteonecrosis of the jaw, esophageal cancer, esophageal ulcers, immune hypersensitivity, arrhythmia, bone fractures, severe muscle pain

Efficacy Monitoring Parameters. Increased BMD. Decreased incidence of bone fractures.

Toxicity Monitoring Parameters. Baseline serum creatinine, calcium, phosphorous. Seek medical attention if severe skin rash, difficulty swallowing, swelling, tooth problems, or severe pain.

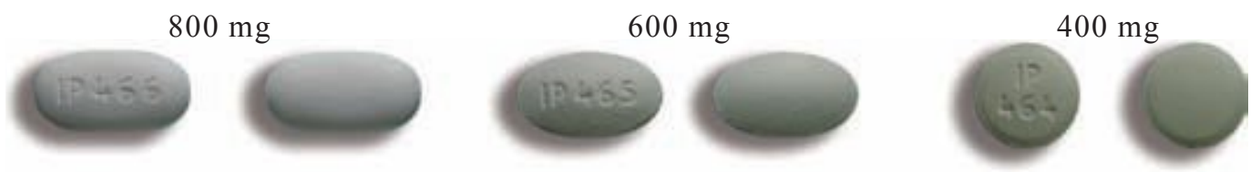
Key Patient Counseling Points. Take this medicine as soon as you get out of bed in the morning, before you eat or have anything to drink. Swallow the tablet whole with a large glass (240 mL) of plain water only (not mineral water, coffee, juice, or any other liquid). Do not take the medicine while you are still in bed, and do not take it at bedtime. Wait for at least 60 min after you swallow the tablet before you eat or drink anything or take any other medicines. This will help your body absorb the medicine. Do not lie down for at least 60 min after taking this medicine, and do not lie down until after you have eaten some food.

Clinical Pearls. Concurrent chemotherapy and poor oral hygiene increase the risk for osteonecrosis of the jaw. Atypical fractures of the thigh (subtrochanteric and diaphyseal femur fractures) have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Given the toxicities, FDA recommends consideration of discontinuation of ibandronate in patients at lower risk of osteoporosis after 3-5 y of therapy. Medication guide required at dispensing. Recommend adjunct calcium and vitamin D if dietary intake is inadequate.

IBUPROFEN: Motrin, Various

Class: NSAID

Dosage Forms. Oral Tablet: 100 mg, 200 mg, 400 mg, 600 mg, 800 mg; **Oral Suspension:** 100 mg/5 mL, 50 mg/1.25 mL, 40 mg/mL; **Oral Capsule:** 200 mg; **Oral Tablet, Chewable**: 50 mg, 100 mg



Amneal generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Fever: Children, 6 mo-12 y of age, 5-10 mg/kg po q6-8h prn; Children ≥12 y of age and Adults, 200-400 mg po q4-6h prn, *max* 1200 mg/d for OTC use
2. Pain, headache: Children, 6 mo-12 y of age, 5-10 mg/kg po q6-8h prn; Children ≥12 y of age and Adults, 200-400 mg po q4-6h prn, *max* 1200 mg/d for OTC use
3. Osteoarthritis or rheumatoid arthritis: 1200-3200 mg/d po in 3-4 divided doses
4. Juvenile rheumatoid arthritis: 30-50 mg/kg/d divided qid, *max* 2400 mg/d

Off-Label Uses. None

MOA. Nonselective inhibitor of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), and reversibly alters platelet function and prolongs bleeding time.

Drug Characteristics: Ibuprofen

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%, minimal food effect
Dose Adjustment Renal	Severe renal dysfunction, avoid	**Distribution**	Vd = 0.1 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	20% hepatic metabolism, CYP2C19 substrate
Pregnancy Category	C (1st and 2nd trimesters); D (3rd trimester)	**Elimination**	45-80% renal elimination with a half-life of 1.8-2.2 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ibuprofen; concurrent use with ketorolac or pentoxifylline; asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain	**Black Box Warnings**	Cardiovascular events, GI toxicity, CABG

Medication Safety Issues: Ibuprofen

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Junior, Migraine, 200, Prin	No	No	No	Halfprin, Neurontin	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent.

Drug Interactions: Ibuprofen

Typical Agents	Mechanism	Clinical Management
Aspirin, low-molecular-weight heparins, SSRIs	Additive GI toxicity and increased risk of bleeding	Monitor for GI toxicity
ACE-Is, angiotensin II receptor blockers, beta-blockers, loop diuretics, thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
Cyclosporine, tacrolimus, lithium	Increased risk of cyclosporine, lithium toxicity, unknown mechanism	Monitor cyclosporine, tacrolimus, or lithium levels and consider dose adjustments
Ketorolac, pentoxifylline	Additive GI toxicity and increased risk of bleeding	Contraindicated
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction
Sulfonylurea antidiabetic agents	Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism	Monitor blood glucose and adjust as necessary
Warfarin	Competitive metabolism	Monitor INR and adjust warfarin dose

Adverse Reactions: Ibuprofen

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity	Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, congestive heart failure, aplastic anemia

Efficacy Monitoring Parameters. Osteoarthritis and rheumatoid arthritis: decreased pain and improved range of motion.

Toxicity Monitoring Parameters. CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

Key Patient Counseling Points. Take with food or milk to decrease GI upset.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs. Various OTC ibuprofen products are available; caution patients not to duplicate dosing with multiple ibuprofen products. Medication guide required at dispensing.

IMIQUIMOD: Zyclara, Various

Class: Immune Response Modifier

Dosage Forms. Topical Cream: 2.5%, 3.75%, 5%

Common FDA Label Indication, Dosing, and Titration.

1. Actinic keratosis: Apply topically to affected treatment area 2 times per week at bedtime for 16 wk
2. Condyloma acuminatum, external: Apply topically to affected area 3 times per week until total clearance or up to a *max* duration of 16 wk
3. Superficial basal cell carcinoma, on trunk, neck, or extremities; when surgical methods are less appropriate and follow-up is assured: Apply topically once daily 5 times per week for 6 wk

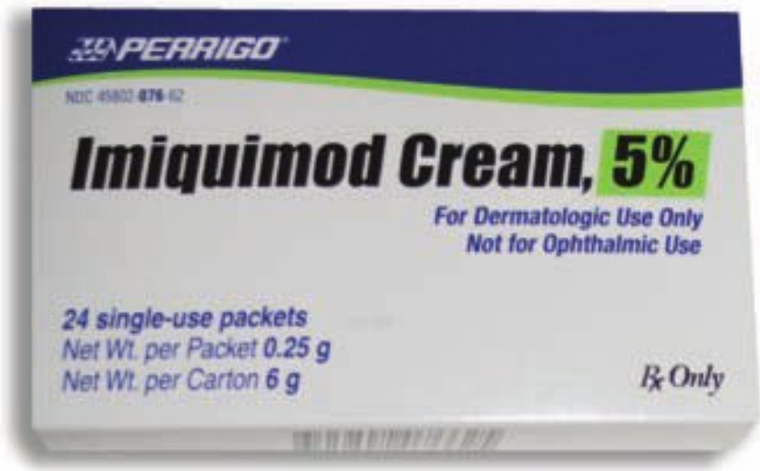
Off-Label Uses.

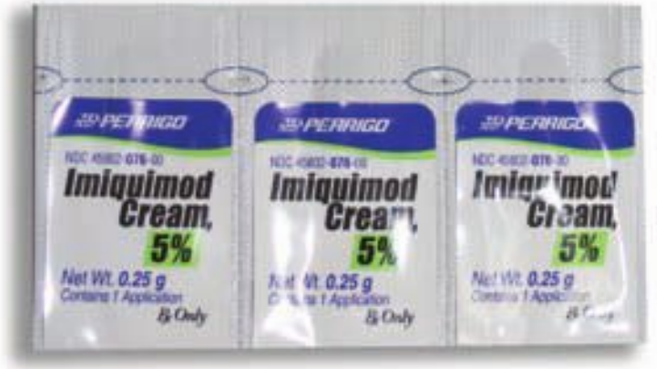
1. Condyloma acuminatum, external-HIV infection: Apply topically to lesion at bedtime 3 times per week on nonconsecutive nights for up to 16 wk; wash with soap and water 6-10 h after each application.

MOA. Toll-like receptor 7 agonist that induces cytokines, including interferon-α and others.

Drug Characteristics: Imiquimod

Dose Adjustment Hepatic	Not required	**Absorption**	Absorption is dose dependent; 75 mg of cream yielded a Cmax = 3.5 ng/mL
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Unknown
Pregnancy Category	C	**Elimination**	Minimal, <1% with a half-life of 20 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	None	**Black Box Warnings**	None





Perrigo generic 5% cream pictured

Medication Safety Issues: Imiquimod

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Zyclara Pump	No	No	No	Alora	No

Drug Interactions: Imiquimod. None known

Adverse Reactions: Imiquimod

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Local itching, burning, and pain	Headache, myalgia	Exfoliative dermatitis

Efficacy Monitoring Parameters. Resolution of skin lesions.

Toxicity Monitoring Parameters. Seek medical attention if signs/symptoms of severe rash, burning, or itching.

Key Patient Counseling Points. Apply at bedtime and leave on skin for 8 h; when you get up, wash the treated skin area with mild soap and water. Do not cover treated skin areas with bandages. Do not use cosmetics or other skin care products on the treated skin areas. Apply on same days of each week. May increase sensitivity to sun.

Clinical Pearls. Condyloma acuminata are also known as genital warts and are sexually transmitted. Patients should be advised to abstain from sex while being treated. Imiquimod is not a cure for genital or anal warts; patients may develop new warts or spread warts while using the cream.

INDOMETHACIN: Indocin, Various

Class: NSAID

Dosage Forms. **Oral Capsule, Immediate Release:** 25 mg, 50 mg; **Oral Capsule, Extended Release:** 75 mg; **Oral Suspension:** 25 mg/5 mL; **Rectal Suppository:** 50 mg

Common FDA Label Indication, Dosing, and Titration.

1. Ankylosing spondylitis, osteoarthritis, rheumatoid arthritis: Immediate Release, 25-50 mg po bid-tid, *max* 200 mg/d; Extended Release, 75 mg po daily bid
2. Pain: Immediate Release, 75-150 mg/d in 3-4 divided doses for 7-14 d

Sandoz generic pictured

Off-Label Uses.

1. Preterm labor, prevention: 25 mg po q6-12h

MOA. Nonselective inhibitor of COX-1 and COX-2, and reversibly alters platelet function and prolongs bleeding time.

Drug Characteristics: Indomethacin

Dose Adjustment Hepatic	Severe hepatic failure, use with caution	**Absorption**	F = 90%, no food effect
Dose Adjustment Renal	CrCl <15 mL/min, use with caution	**Distribution**	Vd = 0.34-1.57 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	40% hepatic
Pregnancy Category	C	**Elimination**	60% renal elimination with a half-life of 4.5 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, concurrent use with ketorolac or pentoxifylline; asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain	**Black Box Warnings**	Cardiovascular events, GI toxicity, CABG

Medication Safety Issues: Indomethacin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	ER capsule	No	Imodium, Lincocin, Minocin, Vicodin	Avoid

Drug Interactions: Indomethacin

Typical Agents	Mechanism	Clinical Management
Aspirin, low-molecular-weight heparins, SSRIs	Additive GI toxicity and increased risk of bleeding	Monitor for GI toxicity
ACE-Is, angiotensin II receptor blockers, beta-blockers, loop diuretics, thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
Cyclosporine, tacrolimus, lithium	Increased risk of cyclosporine, lithium toxicity, unknown mechanism	Monitor cyclosporine, tacrolimus, or lithium levels and consider dose adjustments
Ketorolac, pentoxifylline	Additive GI toxicity and increased risk of bleeding	Contraindicated
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction
Sulfonylurea antidiabetic agents	Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism	Monitor blood glucose and adjust as necessary
Warfarin	Competitive metabolism	Monitor INR and adjust warfarin dose

Adverse Reactions: Indomethacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity	Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated LFTs, acute renal failure, heart failure, aplastic anemia

Efficacy Monitoring Parameters. Osteoarthritis and rheumatoid arthritis: decreased pain and improved range of motion.

Toxicity Monitoring Parameters. CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

Key Patient Counseling Points. Take with food or milk to decrease GI upset.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs. Various OTC NSAID products are available; caution patients not to duplicate dosing with multiple NSAID products. Indomethacin is effective for stopping premature labor and delaying delivery for several weeks, but should be used with caution as it may cause harm to the infant. Medication guide required at dispensing.

INFLUENZA VIRUS VACCINE, INACTIVATED: Afluria, Flublok, Fluzone, Fluzone High-Dose; Fluzone Intradermal, FluLaval, Fluarix, Fluvirin, Flucelvax, Various

Class: Vaccine

Dosage Forms. **Suspension for Intramuscular Injection:** 0.5 mL vial (available as trivalent product containing 2 strains of influenza A virus and 1 influenza B virus strain and as a quadrivalent product containing 2 strains of influenza A virus and 2 influenza B virus strains); **Suspension for Intradermal Injection:** 0.1 mL in prefilled intradermal injection system

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of influenza infection: Adults, 1 dose annual prior to or during influenza season; Children aged 6 mo to 8 y who have not been vaccinated in the past, 2 doses separated by at least 4 wk during the 1st season they receive influenza vaccine

Off-Label Uses. None

Drug Characteristics: Inf uenza Virus Vaccine, Inactivated

Pregnancy Category	C	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to inf uenza vaccine, egg protein or a component of the vaccine; asthma, chronic medical conditions, immunosuppression	**Black Box Warnings**	None

Medication Safety Issues: Inf uenza Virus Vaccine, Inactivated

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Flumazenil; vials and syringes often mistaken for tetanus toxoid or tuberculin skin test	No

Sanofi Pasteur pictured

I

Drug Interactions: Inf uenza Virus Vaccine, Inactivated

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression and increased risk of infection by vaccine	Delay vaccine administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents, including cyclosporine, cancer chemotherapy	Immunosuppression and increased risk of infection by vaccine	Delay vaccine administration until corticosteroid therapy has been discontinued if possible

Adverse Reactions: Inf uenza Virus Vaccine, Inactivated

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Itching, fatigue, headache, nasal congestion	Fever, myalgia, arthralgia	Anaphylaxis, Guillain-Barré syndrome, febrile seizures

Efficacy Monitoring Parameters. Prevention of influenza infection.

Toxicity Monitoring Parameters. Syncope.

Key Patient Counseling Points. Annual seasonal immunization is recommended.

Clinical Pearls. Choose the vaccine preparation for appropriate age group. Use current year vaccine only (virus strains and vaccine vary year to year). Not all influenza vaccines are licensed for young children. Intradermal influenza vaccine licensed for adults aged 18-64 y. High-dose influenza vaccine licensed for individuals aged ≥65 y. Flublok is a recombinant influenza vaccine for ages 18-49 y and can be used in egg-allergic individuals. Flucelvax vaccine virus is grown in cell culture, but the seed virus is grown in eggs. Afluria is not recommended for children <9 y of age due to risk of febrile seizures. Recommended for pregnant females.

INFLUENZA VIRUS VACCINE, LIVE: FluMist, Quadrivalent

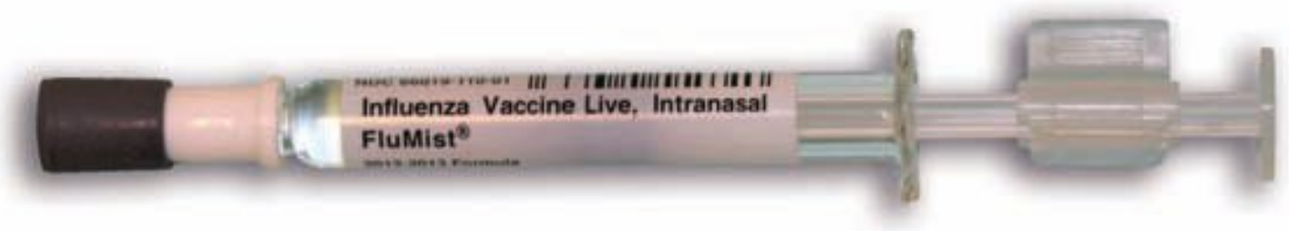
Class: Vaccine

Dosage Forms. **Intranasal Spray:** 0.2 mL (quadrivalent product containing 2 strains of influenza A virus and 2 influenza B virus strains)

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of influenza infection: Adults, healthy, aged 18-49 y, 1 spray each nostril annually; Children, healthy, aged 2-18 y, 1 spray in each nostril annually
2. Preferred influenza vaccine preparation for healthy children aged 2-8 y

Off-Label Uses. None



MedImmune pictured

Drug Characteristics: Inf uenza Virus Vaccine, Live

Pregnancy Category	B	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to inf uenza vaccine, egg protein or a component of the vaccine; asthma, chronic medical conditions, immunosuppression; pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Inf uenza Virus Vaccine, Live

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Flumazenil	No

Drug Interactions: Inf uenza Virus Vaccine, Live

Typical Agents	Mechanism	Clinical Management
Aspirin, salicylates	Increased risk of Reye syndrome	Avoid giving salicylates to children for the 6 wk following live inf uenza virus vaccine administration
Moderate- to high-dose corticosteroids	Immunosuppression and increased risk of infection by vaccine	Delay live inf uenza virus vaccine administration until corticosteroid therapy has been discontinued
Immunosuppressing agents, including cyclosporine, cancer chemotherapy	Immunosuppression and increased risk of infection by vaccine	Delay live inf uenza virus vaccine administration until immunosuppressive therapy has been discontinued
Inf uenza antiviral medications: adamantanes, neuraminidase inhibitors	Interference with immune response to inf uenza virus vaccine	Hold antiviral agent for at least 2 wk

Adverse Reactions: Inf uenza Virus Vaccine, Live

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, nasal congestion	Fever	Anaphylaxis, Guillain-Barré syndrome, Bells palsy

Efficacy Monitoring Parameters. Prevention of influenza infection.

Toxicity Monitoring Parameters. Nasal discharge.

Key Patient Counseling Points. Annual seasonal immunization is recommended.

Clinical Pearls. Use current year vaccine only (virus strains and vaccine vary year to year). LAIV has an 18-wk expiration date so it can expire before the end of the season. Transmission of the vaccine virus to susceptible individuals without clinical consequences has been documented. Avoid administering to contacts of individuals so severely immunocompromised that they require protective isolation. The dose is sprayed into each nostril with no cooperation (active inhalation) required by the individual being vaccinated. Vaccine dosing does not need to be repeated if the individual sneezes following administration.

INSULIN: Humulin R, Humulin N, Humulin 70/30, Various

Class: Insulin, Short-Acting (R); Intermediate-Acting (NPH)

Dosage Forms. **Injection Solution:** Humulin R (Regular): 100 units/mL, 500 units/mL; Humulin N (NPH): 100 units/mL; Humulin 70/30 (NPH/Regular): 70 units NPH/30 units Regular/mL

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 1 and 2: Subcutaneous dosing is individualized to patient needs

Off-Label Uses. None

MOA. Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Drug Characteristics: Insulin

Dose Adjustment Hepatic	Not required	**Absorption**	Regular: onset: 30 min, peak effect: 2 h, duration: 4-6 h; NPH: onset: 2 h, peak effect: 4-8 h, duration: 8-12 h
Dose Adjustment Renal	Not required	**Distribution**	Protein binding 5%
Dialyzable	Not dialyzable	**Metabolism**	50% hepatic, 30% renal, 20% adipose tissue
Pregnancy Category	Not categorized, but used in pregnancy	**Elimination**	Renal elimination is 30% with a half-life of 1-5 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Lilly NPH 100 units/mL pictured

Medication Safety Issues: Insulin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
R = Regular, N = NPH, 70/30 = 70% NPH/30% R, U-500 (high concentration)	HumuLIN, NovoLIN	No	Yes	HumaLOG, HumuLIN, NovoLIN, NovoLOG	Avoid sliding scale

Drug Interactions: Insulin

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Insulin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, weight gain	Hypoglycemia, lipodystrophy	Severe hypersensitivity, insulin resistance, severe hypoglycemia

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

Clinical Pearls. Beef and pork insulins are extracted and purified from the animal's pancreas. Human insulin is produced by recombinant DNA technology or enzymatic conversion of pork insulin. No differences in side effects or long-term control of diabetes have been observed between human insulin and highly purified pork insulin. Use caution when dispensing 500 units/mL insulin solution, can result in accidental overdose of insulin and hypoglycemia. Regular is short acting; NPH is intermediate acting. Rapid acting inhaled insulin was approved by FDA in June 2014, but is not yet available.

INSULIN ASPART: NovoLog, NovoLog FlexPen

Class: Insulin, Rapid-Acting

Dosage Forms. Injection Solution: 100 units/mL; **Pen and Refills (Administration Device)**: 100 units/mL

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

Off-Label Uses. None

MOA. Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Novo Nordisk pictured

Drug Characteristics: Insulin Aspart

Dose Adjustment Hepatic	Not required	**Absorption**	Onset: 15-30 min, peak: 1-2 h, duration: 3-5 h
Dose Adjustment Renal	Not required	**Distribution**	Protein binding 5%
Dialyzable	Not dialyzable	**Metabolism**	50% hepatically metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 30% with a half-life of 1.5 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Insulin Aspart

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
FlexPen, FlexFill	NovoLOG	No	Yes	HumaLOG, HumuLIN, Nimbex, NovoLIN, NovoLOG Mix 70/30	Avoid sliding scale

Drug Interactions: Insulin Aspart

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Insulin Aspart

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, weight gain, hypoglycemia	Pruritus, rash, lipodystrophy	Severe hypersensitivity, insulin resistance

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

Clinical Pearls. Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. This is the fastest acting insulin.

INSULIN DETEMIR: Levemir

Class: Insulin, Long-Acting

Dosage Forms. Injection Solution: 100 units/mL; **Pen (Administration Device):** 100 units/mL

Common FDA Label Indication and Dosing.

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

Off-Label Uses. Not required

MOA. Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Drug Characteristics: Insulin Detemir

Dose Adjustment Hepatic	Not required	**Absorption**	Onset: 2 h, no peak, duration: 14-24 h (dose dependant)
Dose Adjustment Renal	Not required	**Distribution**	98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	50% hepatically metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 30% with a half-life of 5-7 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Insulin Detemir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
FlexPen, FlexTouch	No	No	Yes	FlexFill	Avoid sliding scale

Novo Nordisk 100 units/mL pictured

Drug Interactions: Insulin Detemir

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Insulin Detemir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, weight gain, hypoglycemia	Pruritus, rash	Severe hypersensitivity, insulin resistance

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites. Not for IV or IM use. Do not share pens, even if needles are changed.

Clinical Pearls. Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust.

INSULIN GLARGINE: Lantus

Class: Insulin, Long-Acting

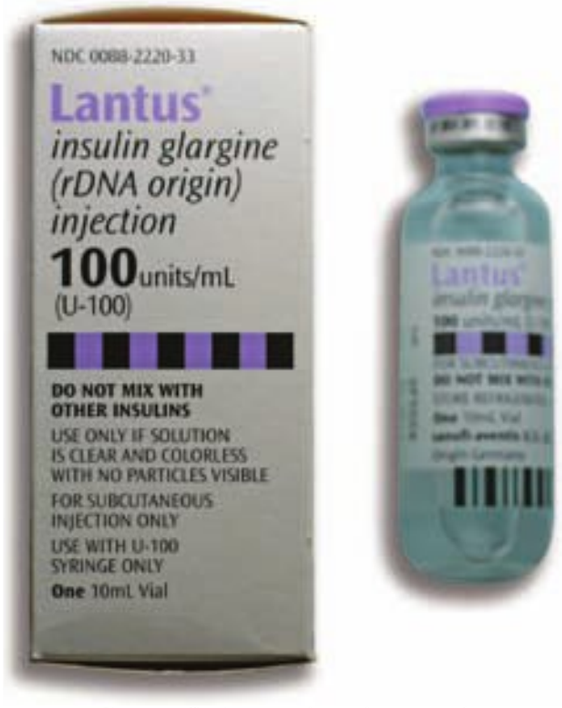
Dosage Forms. Injection Solution: 100 units/mL

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

Off-Label Uses. None

MOA. Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.



Sanofi-Aventis pictured

Drug Characteristics: Insulin Glargine

Dose Adjustment Hepatic	Not required	**Absorption**	Onset: 4-5 h, peak: none, duration: 22-24 h
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Metabolized to form active metabolites: M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin) 50%
Pregnancy Category	C	**Elimination**	Duration of effect 10-24 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Insulin Glargine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
SoloStar	No	No	Yes	Latanoprost, Latuda, Xalatan	Avoid sliding scale

Drug Interactions: Insulin Glargine

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible, monitor and consider dose adjustments

Adverse Reactions: Insulin Glargine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, weight gain, hypoglycemia	Pruritus, rash, lipodystrophy	Severe hypersensitivity, insulin resistance

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

Clinical Pearls. Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. Following subcutaneous administration, insulin glargine forms a microprecipitate in the fatty tissue from which small amounts of insulin are released slowly, resulting in a relatively constant concentration/time profile over 24 h with no pronounced peak.

INSULIN LISPRO: Humalog, Humalog KwikPen

Class: Insulin, Rapid-Acting

Dosage Forms. **Injection Solution:** 100 units/mL; **Pen (Administration Device):** 100 units/mL

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

Off-Label Uses. None

MOA. Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Lilly pictured 100 units/mL

Drug Characteristics: Insulin Lispro

Dose Adjustment Hepatic	Not required	**Absorption**	Onset: 15-30 min, peak: 1-2 h, duration 3-4 h
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.26 L/kg
Dialyzable	Not dialyzable	**Metabolism**	50% hepatically metabolized
Pregnancy Category	C	**Elimination**	Half-life of 0.5-1 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Insulin Lispro

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Mix 50/50, KwikPen	HumaLOG	No	Yes	Humira, HumaLIN N, HumaLIN R, NovoLOG	Avoid sliding scale

Drug Interactions: Insulin Lispro

Typical Agents	Mechanism	Clinical Management
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Somatostatin analogues	Altered glucose metabolism and increased risk of hypoglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible, monitor and consider dose adjustments

Adverse Reactions: Insulin Lispro

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, weight gain, hypoglycemia	Hypokalemia, lipodystrophy	Severe hypersensitivity, insulin resistance

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

Clinical Pearls. Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. Injection of insulin lispro into an abdominal versus posterior upper arm or lateral thigh area site results in more rapid absorption. Faster acting than regular insulin.

IPRATROPIUM/ALBUTEROL: Combivent, Various

Class: Anticholinergic/Selective β_2-Agonist Combination

Dosage Forms. **Metered-Dose Inhaler (MDI):** 18 mcg/90 mcg ipratropium/albuterol per actuation; **Inhalation Solution:** 0.5 mg/2.5 mg ipratropium/albuterol per 3 mL; **Spray:** 20 mcg/100 mcg ipratropium/albuterol per inhalation

Common FDA Label Indication, Dosing, and Titration.

1. Chronic obstructive pulmonary disease: Adults, 2 inhalations qid (*max* 12 inhalations/d) or 3 mL via nebulizer qid (*max* 6 doses/d)

Off-Label Uses.

1. Asthma exacerbation: Adults, ipratropium 0.5 mg with albuterol 2.5 mg via nebulized usually given once

MOA. Albuterol is a selective β_2-adrenergic agonist that produces bronchodilation, vasodilation, uterine relaxation, skeletal muscle stimulation, peripheral vasodilation, and tachycardia. Ipratropium is a competitive antagonist of acetylcholine at peripheral, but not central, muscarinic receptors. It appears to produce bronchodilation by inhibition of cholinergic receptors on bronchial smooth muscle.

Boehringer Ingelheim pictured

Drug Characteristics: Ipratropium/Albuterol

Dose Adjustment Hepatic	Not required	**Absorption**	About 90% of an inhaled dose is swallowed; F = 6.9% following inhalation
Dose Adjustment Renal	Not required	**Distribution**	Albuterol protein binding 10%
Dialyzable	Not dialyzable	**Metabolism**	Albuterol is conjugatively metabolized to an active metabolite; ipratropium is partially metabolized to 8 inactive metabolites
Pregnancy Category	C	**Elimination**	Albuterol renal elimination is 80-100% with a half-life of 4 h; ipratropium has minimal renal elimination, 48% in feces, with a half-life of 2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to albuterol, ipratropium, or any other components of the product, or to atropine or its derivatives, or levalbuterol; hypersensitivity to soya lecithin or related food products (eg, soybean, peanut products)	**Black Box Warnings**	None

Medication Safety Issues: Ipratropium/Albuterol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Combivir, Serevent	No

Drug Interactions: Ipratropium/Albuterol

Typical Agents	Mechanism	Clinical Management
Other anticholinergic agents	Additive effect with ipratropium	Avoid concurrent use
Other short-acting sympathomimetics	Additive effect with albuterol	Avoid concurrent use
Beta-blockers	May decrease effectiveness of albuterol and produce bronchospasms	Avoid use of nonselective beta-blocker in patients with asthma; monitor PFTs if cardioselective beta-blockers are clinically indicated
Diuretics (non-potassium sparing)	May potentiate hypokalemia	Monitor potassium levels
Digoxin	May decrease digoxin levels	Monitor digoxin levels
MAOI and tricyclic antidepressants	May potentiate albuterol effect on cardiovascular system	Consider alternative therapy

Adverse Reactions: Ipratropium/Albuterol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bronchitis, upper respiratory tract infections	Angina, tachycardia, nausea, cough, headache, dyspnea, tremor, nervousness, insomnia, urinary retention, blurred vision	Angle-closure glaucoma, pneumonia, hypersensitivity reactions, paradoxical bronchospasm

Efficacy Monitoring Parameters. Resolution of COPD symptoms, improved PFTs.

Toxicity Monitoring Parameters. Use alternative therapy or seek emergency treatment if paradoxical bronchospasms occur.

Key Patient Counseling Points. Instruct patient on appropriate inhaler technique. Wash the mouthpiece in warm water and air dry thoroughly daily (may cease to deliver medication if mouthpiece becomes blocked). Store the inhaler at room temperature; avoid excessive humidity; do not freeze. Each canister contains 200 inhalations. Keep track of number of inhalations administered and discard canister after 200 inhalations have been used. Nebulizer technique: use entire vial of inhalation solution immediately after opening to avoid contamination; deliver over 5-15 min. Seek medical attention if the prescribed dose does not provide relief or if symptoms worsen.

Clinical Pearls. Because of anticholinergic effect of ipratropium, use with caution in patients with bladder neck obstruction, narrow-angle glaucoma, or BPH.

IRBESARTAN: Avapro, Various

Class: Angiotensin II Receptor Antagonist

Dosage Forms. Oral Tablet: 75 mg, 150 mg, and 300 mg

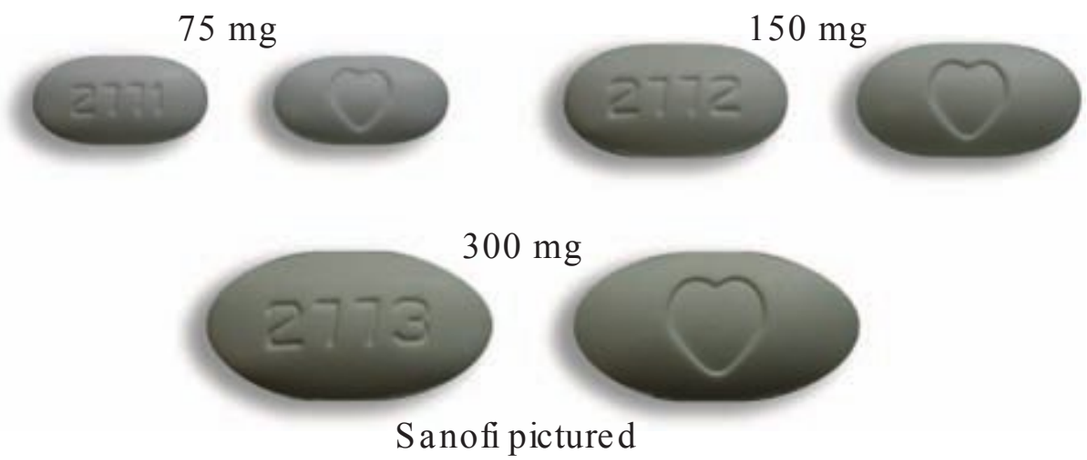
Common FDA Label Indication, Dosing, and Titration.

1. Diabetic nephropathy in patients with type 2 diabetes and hypertension: Adults, 75-300 mg po daily; titrate to target dose of 300 mg daily
2. Hypertension: Adults, initial, 150-300 mg po daily

Off-Label Uses.

1. Left ventricular hypertrophy: Adults, 150-300 mg po daily
2. Hypertension, renal impairment: Adults, 150-300 mg po daily

MOA. Irbesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1), which is responsible for the physiologic effects of angiotensin II including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.



Sanofi pictured

Drug Characteristics: Irbesartan

Dose Adjustment Hepatic	Not required	**Absorption**	F = 80%, food does not affect absorption
Dose Adjustment Renal	Patients receiving hemodialysis, initial dose 75 mg po daily	**Distribution**	Vd = 53-93 L; 90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minor CYP2C9 substrate. Moderate inhibitor of CYP2C8 and CYP2C9
Pregnancy Category	C (1st trimester), D (2nd and 3rd trimesters)	**Elimination**	Renal elimination is 20% and fecal elimination is 80% with a half-life 11-15 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity or pregnancy	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Irbesartan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Anaprox	No

Drug Interactions: Irbesartan

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
CYP2C8 and 2C9 substrates	Decreased metabolism of substrates and increased toxicity of substrates	Avoid concurrent use or consider substrate dose reduction
ACE-Is	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive and natriuretic effect of irbesartan, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly
Lithium	Increased risk of lithium toxicity	Monitor serum lithium levels

Adverse Reactions: Irbesartan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Diarrhea, dizziness, fatigue, heartburn, hyperkalemia, hypotension, nephrotoxicity, tachycardia	Angioedema, birth defects, hepatotoxicity, rhabdomyolysis

Efficacy Monitoring Parameters. Decreased BP. Monitor BP weekly; may require 2-4 wk for full effect.

Toxicity Monitoring Parameters. Report signs/symptoms of hypotension, tachycardia. Baseline and periodic electrolyte panel, renal function tests, and urine protein are recommended.

Key Patient Counseling Points. Seek medical attention if angioedema (swelling of the face, eyes, lips, tongue, or throat), excessive fluid loss (vomiting, diarrhea, or excessive perspiration), hyperkalemia (confusion, body weakness, uneven heartbeat, or numbness/tingling in hands or feet), reduction in urination, jaundice, or skin rash occurs. Avoid pregnancy. Avoid abrupt discontinuation. Use potassium supplements or salt substitutes only under medical supervision. This medicine may cause dizziness. Avoid alcohol or driving.

Clinical Pearls. Safety and efficacy have not been established in children.

ISOSORBIDE MONONITRATE: Imdur, ISMO, Monoket, Various

Class: Long-Acting Nitrate, Anti-anginal

Dosage Forms. **Oral Tablet, Extended Release:** 30 mg, 60 mg, 120 mg; **Oral Tablet, Immediate Release:** 10 mg, 20 mg

Kremers Urban generic 20 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Angina, prophylaxis: Adults, Extended Release, initial, 30-60 mg po daily, may titrate to maintenance of 120-240 mg po daily; Immediate Release, 20 mg bid separated 7 h apart to decrease tolerance development

Off Label Uses. None

MOA. Isosorbide mononitrate (ISMN) is the active 5-mononitrate metabolite of isosorbide dinitrate. Nitroglycerin and other organic nitrates are converted to nitric oxide (NO) by vascular endothelium. NO activates guanylate cyclase, increasing cyclic GMP that in turn decreases intracellular calcium, resulting in direct relaxation of vascular smooth muscle.

Drug Characteristics: Isosorbide Mononitrate

Dose Adjustment Hepatic	Not required	**Absorption**	F = 93%, food slows rate (but not extent) of absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.6L; <5% protein bound
Dialyzable	Yes (hemodialysis)	**Metabolism**	>95% hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination of metabolites is 96% with a half-life of 6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nitrates, concurrent use with erectile dysfunction meds	**Black Box Warnings**	None

Medication Safety Issues: Isosorbide Mononitrate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	XR formulation	No	Imuran, Inderal LA, K-Dur	No

Drug Interactions: Isosorbide Mononitrate

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased metabolism of isosorbide mononitrate decreases isosorbide efficacy	Monitor for toxicity and consider dose increases of isosorbide mononitrate
CYP3A4/5 inhibitors	Decreased metabolism of isosorbide mononitrate increases risk of isosorbide mononitrate toxicity	Monitor for efficacy and consider dose decreases of isosorbide mononitrate
Phosphodiesterase inhibitors (erectile dysfunction medications)	Excessive hypotension	Concurrent use contraindicated; separate sildenafil and vardenafil from nitrates by 24 h; tardenafil from nitrates by 48 h

Adverse Reactions: Isosorbide Mononitrate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, headache	Bradycardia, f ushing, hypotension, nausea, orthostatic hypotension, tachycardia, vomiting	Severe hypotension, syncope

Efficacy Monitoring Parameters. Decreased use of sublingual nitroglycerin, reduction in angina episodes.

Toxicity Monitoring Parameters. Report signs/symptoms of hypotension, problematic headaches, or decreasing efficacy (drug tolerance) to prescriber.

Key Patient Counseling Points. It is best to take this medicine on an empty stomach with at least half a glass of water. Swallow the extended-release tablet whole. Do not break, crush, or chew it. This medicine can cause headaches, which is a sign that the medicine is working. Acetaminophen may be used to relieve the headache. Talk with your doctor if the headache is severe. This medicine can cause dizziness. Avoid driving, using machines, or doing anything else that could be dangerous if not alert. Stand up slowly if this medicine causes light-headedness from orthostatic hypotension. Do not stop using this medicine suddenly without asking a health-care provider. The dose may need to be slowly decreased before stopping it completely. Avoid concomitant use of erectile dysfunction medications as this may increase risk of severe hypotension. Avoid drinking alcohol while taking this drug.

Clinical Pearls. Safety and efficacy have not established in children. Combining long-acting nitrates with antihypertensive medications can increase risk of hypotension. To avoid tolerance, include an 8-h nitrate-free interval in every 24-h period.

KETOCONAZOLE TOPICAL: Nizoral, Various

Teva generic 2% cream pictured

Class: Imidazole Antifungal

Dosage Forms. **Topical Cream:** 2%, **Topical Foam:** 2%, **Topical Gel:** 2%, **Topical Shampoo:** 1% (OTC), 2% (by prescription)

Common FDA Label Indication, Dosing, and Titration.

1. Candidiasis of skin: Apply 2% cream topically once daily for 2 wk
2. Dandruff: Apply 1% shampoo topically to wet hair, lather, rinse thoroughly, and repeat; use every 3-4 d for up to 8 wk; then as needed to control dandruff
3. Pityriasis versicolor: Apply 2% shampoo topically to damp skin and a wide surrounding margin, lather, leave on skin for 5 min, then rinse, *or* apply 2% cream to affected areas once daily × 2 wk
4. Seborrheic dermatitis: Apply cream, gel, and foam topically to the affected area bid for 4 wk or until clinical clearing
5. Tinea corporis: Apply 2% cream topically once daily for 2 wk
6. Tinea cruris: Apply 2% cream topically once daily for 2 wk
7. Tinea pedis: Apply 2% cream topically once daily for 6 wk

Off-Label Uses. None

MOA. Ketoconazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability.

Drug Characteristics: Ketoconazole Topical

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption
Dose Adjustment Renal	Not required	**Distribution**	Minimal absorption
Dialyzable	Not dialyzable	**Metabolism**	Minimal absorption
Pregnancy Category	C	**Elimination**	Minimal absorption
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Ketoconazole Topical

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
A-D	No	No	No	Nasarel, Neoral, Nitrol	No

Drug Interactions: Ketoconazole Topical. None known with topical product; many interactions with oral formulation

Adverse Reactions: Ketoconazole Topical

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Application site reaction with foam	Dry skin, burning, stinging at site of application	Rash, hair loss

Efficacy Monitoring Parameters. Resolution of erythema and pruritus. Improvement in erythema and pruritus usually occurs within 3-5 d. If no improvement is seen after 1 wk of treatment for tinea cruris or tinea corporis or after 2 wk of treatment for tinea pedis, then the diagnosis should be reviewed.

Toxicity Monitoring Parameters. Seek medical attention if severe skin irritation or rash.

Key Patient Counseling Points. Apply thin layer to affected area of skin. Skin should be intact. Do not get it in your eyes, nose, mouth, or vagina. Do not wash the areas where you applied this medicine for at least 3 h after application. Cosmetics (makeup or sunscreens) may be put on the affected areas 20 min after application. Topical products are alcohol based and flammable immediately after application.

Clinical Pearls. Topical products typically not effective in toenail onychomycosis. Resistant infections typically require oral therapy.

LABETALOL: Normodyne, Various

Class: α/β-Adrenergic Blocker

Dosage Forms. Oral Tablet: 100 mg, 200 mg, 300 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, initial, 100 mg po bid; may titrate in 100 mg increments po bid every 2-3 d to maintenance dose of 200-400 mg po bid, *max* dose 2400 mg daily

Off-Label Uses.

1. Hypertension: Children, initial, 1-3 mg/kg/d po in 2 divided doses; *max* 10-12 mg/kg/d or 600 mg po bid
2. Hypertension, urgency: 200-400 mg po depending on initial BP

MOA. Labetalol is an adrenergic receptor blocking drug that has selective α_1- and nonselective β-adrenergic receptor blocking actions.

Drug Characteristics: Labetalol

Dose Adjustment Hepatic	Reduce dose by 50% if hepatic failure	**Absorption**	F = 25%; food increases absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3-16 L/kg; 50% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic and primarily via glucuronide conjugation
Pregnancy Category	C	**Elimination**	Renal elimination is 55-60% (5% unchanged) and 50% in feces, with a half-life of 5-8 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity; bronchial asthma or related bronchospastic condition; severe sinus bradycardia, 2nd- or 3rd-degree AV block; overt heart failure; cardiogenic shock, conditions associated with severe and prolonged hypotension	**Black Box Warnings**	None

Medication Safety Issues: Labetalol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes (IV only)	Betaxolol, lamoTRIgine, Lipitor	No

Drug Interactions: Labetalol

Typical Agents	Mechanism	Clinical Management
Alpha-/Beta-agonists	Labetalol may enhance the vasopressor effect of alpha-/beta-agonist	Avoid concurrent use or monitor BP
Alpha1-blockers, fentanyl	Additive orthostatic hypotension	Avoid concurrent use or monitor BP
Beta-blockers, amiodarone, dronedarone	Increased risk of bradycardia, heart block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
Antidiabetic drugs	Decreased glycemic control	Monitor blood glucose levels
Calcium channel blockers	Increased risk of hypotension and/or bradycardia and AV block	Avoid concurrent use

Adverse Reactions: Labetalol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, fatigue, nausea	Bradyarrhythmias, constipation, diaphoresis, diarrhea, disorder of glucose regulation, dyspnea, headache, impotence, increased liver enzymes, orthostatic hypotension, somnolence, wheezing	Hepatotoxicity, bronchospasm

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema, increased HR, signs/symptoms of liver damage.

Key Patient Counseling Points. Report signs/symptoms of hypotension with initial dosing and dose changes. Avoid alcohol while taking drug. May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Instruct patient to rise slowly from a sitting/supine position, as labetalol may cause orthostatic hypotension. Report signs/symptoms of bronchospasm, slow HR, hepatotoxicity, or syncope. Advise diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia. Advise patients against sudden discontinuation of drug as this may cause rebound hypertension.

Clinical Pearls. Safety and efficacy not established in pediatric patients <6 y of age. Is not a first-line agent for managing hypertension, thiazides, calcium channel blockers are preferred for initial management

LACOSAMIDE: Vimpat

Class: Anticonvulsant, Miscellaneous. C-V

Dosage Forms. **Oral Tablet:** 50 mg, 100 mg, 150 mg, 200 mg; **Oral Solution:** 10 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Partial onset seizure: Initial, 100 mg po bid, may titrate by 50 mg increments to *max* of 200 mg po bid

Off-Label Uses. None

MOA. Lacosamide stabilizes hyperexcitable neuronal membranes and inhibits neuronal firing

Drug Characteristics: Lacosamide

Dose Adjustment Hepatic	*Max* dose 300 mg in mild to moderate hepatic dysfunction, avoid in severe hepatic dysfunction	**Absorption**	F = 100%
Dose Adjustment Renal	CrCl ≤30 ml/min, *max* dose is 300 mg	**Distribution**	Vd = 0.6 L/kg
Dialyzable	Removed by hemodialysis	**Metabolism**	Hepatic, CYP3A4/5, 2C9 and 2C19 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 95% (40% unchanged) with a half-life of 13 h
Lactation	Excretion into breast milk unknown, weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Lacosamide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zonisamide	No

Drug Interactions: Lacosamide

Typical Agents	Mechanism	Clinical Management
CYP2C9, CYP3A4/5 inhibitors	Decreased lacosamide metabolism increases risk of lacosamide toxicity	Consider dose decreases of lacosamide if concurrent strong CYP3A4/5 or CYP2C9 inhibitors or poor renal or hepatic function, monitor and consider dose reduction if concurrent moderate inhibitors
CYP2C9, CYP3A4/5 inducers	Increased lacosamide metabolism decreases lacosamide efficacy	Consider dose increases of lacosamide if concurrent strong CYP3A4/5 or CYP2C9 inhibitors, monitor and consider dose increase if concurrent moderate inhibitors

Adverse Reactions: Lacosamide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, fatigue, ataxia, nausea, tremor, diplopia	Syncope, drowsiness, diarrhea, pruritus, nystagmus, increased liver enzymes	Acute psychosis, bradycardia, hepatotoxicity, agranulocytosis, suicidiality

Efficacy Monitoring Parameters. Decreased seizures.

Toxicity Monitoring Parameters. Obtain ECG prior to initiating therapy in patients with underlying risk of conduction disorders. CBC, LFTs and SCr at initiation and periodically during therapy.

Key Patient Counseling Points. May be taken without regard to food but at same time of day. Take with food if GI distress. For the oral solution, measure carefully with oral syringe. Seek medical attention if seizure frequency increases or seizures worsen, abnormal heartbeat or extreme dizziness.

Clinical Pearls. May be used as monotherapy or added to other antiseizure medications for patients with resistant epilepsy. Start at 50 mg when used in combination.

LAMOTRIGINE: Lamictal, Various

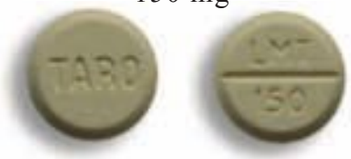
Class: Phenyltriazine Anticonvulsant

Dosage Forms. **Oral Chewable Tablet:** 2 mg, 5 mg, 25 mg; **Oral Tablet:** 25 mg, 100 mg, 150 mg, 200 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 100 mg, 200 mg, 250 mg, 300 mg; **Oral Dispersible Tablet:** 25 mg, 50 mg, 100 mg, 200 mg

200 mg

Teva generic pictured

150 mg



Taro generic pictured

100 mg

Taro generic pictured

25 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar I disorder: Adults, 100-400 mg po daily
2. Partial seizure, adjunct or monotherapy, tonic-clonic seizure, Lennox-Gastaut syndrome, adjunctive: Adults and Children ≥12 y of age, Immediate Release, 100-500 mg/d po in 2 divided doses, Extended Release, 200-600 mg po daily; Children 2-12 y of age: Immediate Release, 1-15 mg/kg/d po in 1 or 2 divided doses, *max* 400 mg/d

Off-Label Uses. None

MOA. Lamotrigine is a phenyltriazine derivative unrelated to other marketed antiepileptic drugs (AEDs). Lamotrigine inhibits voltage-dependent sodium channels, thereby stabilizing neuronal membranes and reducing the release of excitatory neurotransmitters such as glutamate and aspartate.

Drug Characteristics: Lamotrigine

Dose Adjustment Hepatic	Moderate-severe without ascites, reduce dose by 25%; severe with ascites, reduce dose by 50%	**Absorption**	F = 98%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.9-1.3 L; 55% protein bound
Dialyzable	Yes (hemodialysis), 20% removed	**Metabolism**	90% hepatic and occurs by glucuronidation
Pregnancy Category	C	**Elimination**	Renal elimination is 94% with a half-life of 25-70 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	Skin reactions

Medication Safety Issues: Lamotrigine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ODT, XR	LamoTRIgine, LaMICtal	Extended-release formulation, oral dispersible tablet	No	Labetalol, LamISIL, lamiVUDine, levothyroxine, Lomotil	No

Drug Interactions: Lamotrigine

Typical Agents	Mechanism	Clinical Management
Enzyme inducers, rifampin, carbamazepine	Increased lamotrigine metabolism decreases lamotrigine efficacy	Monitor seizure control and consider dose increase of lamotrigine
Escitalopram	Increased risk of myoclonus through additive effect on calcium channels	Caution with concurrent use
Ethinyl estradiol and other estrogen-based birth control products	Decreased lamotrigine concentrations via increased metabolism	Use an alternative form of birth control or consider dose increase of lamotrigine
Risperidone	Increased risperidone plasma concentrations and risk of adverse effects via unknown mechanism	Monitor and use with caution

Adverse Reactions: Lamotrigine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Rash, ataxia, somnolence, headache, diplopia, rhinitis, nausea, vomiting, insomnia	Vertigo, anxiety, depression, dysmenorrhea	Stevens-Johnson syndrome, anemia, leukopenia, disseminated intravascular coagulation, thrombocytopenia, liver failure, aseptic meningitis, suicidal thoughts

Efficacy Monitoring Parameters. Seizure severity and frequency if taken for seizures. Decrease in manic or depressive symptoms if for bipolar disorder.

Toxicity Monitoring Parameters. Seek medical attention if yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

Key Patient Counseling Points. Seek medical attention if rash develops. Slow titration necessary to minimize side effects. Avoid alcohol. Talk to your health-care provider if you become or plan to become pregnant. Review driving restrictions for patients with seizures. Place oral disintegrating tablet formulation on tongue and allow to dissolve.

Clinical Pearls. Rash is more common in children, when quickly titrated and with high starting doses. Rash usually occurs 2-8 wk after start of therapy. Extended-release products are not approved for use in children <13 y of age. Bipolar patients have an increased risk of suicide during first 24 wk of therapy. Avoid abrupt discontinuation, increases risk of seizures. Medication guide required at dispensing.

LANSOPRAZOLE: Prevacid, Various

Class: Proton Pump Inhibitor

Dosage Forms. Oral Capsule, Delayed Release: 15 mg, 30 mg; **Oral Disintegrating Tablet:** 15 mg, 30 mg; **Powder for Oral Suspension:** 3 mg/mL

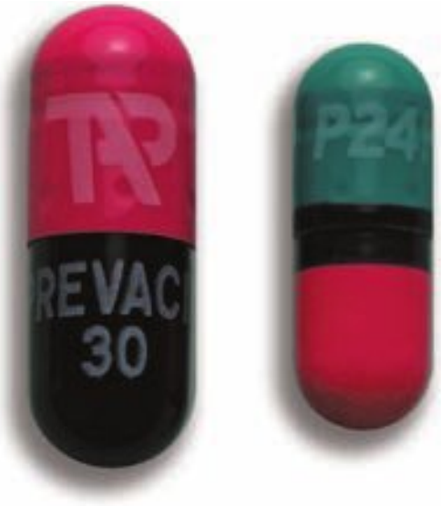
Common FDA Label Indication, Dosing, and Titration.

1. Duodenal ulcer disease: 15 mg po daily × up to 4 wk
2. Gastric ulcer disease, treatment: 30 mg po daily × up to 8 wk
3. *Helicobacter pylori* GI tract infection, triple therapy: 30 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
4. Erosive esophagitis, GERD, treatment: Children 1-11 y of age and ≤30 kg, 15 mg po daily × 12 wk; Children >30 kg, 30 mg po daily × 12 wk; Children ≥12 y of age and Adults, 30 mg po daily × 8-16 wk
5. Zollinger-Ellison syndrome: 60 mg po bid up to 180 mg/d

Off-Label Uses.

1. Heartburn ≥2 d/wk: 15 mg po daily for up to 14 d (OTC labeling)
2. Drug-induced GI disturbance: 15 mg po daily

Takeda generic 30 mg pictured



Novartis 15 mg pictured

MOA. Lansoprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^{++}/K+-ATPase (proton pump), which is the final pathway for acid secretion.

Drug Characteristics: Lansoprazole

Dose Adjustment Hepatic	Consider dose adjustments in severe liver disease	**Absorption**	F = 80%, brief delay in reaching peak if taken with food, but no effect of food on overall absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 14-18 L; 97% protein bound
Dialyzable	Not dialyzable	**Metabolism**	70-75% hepatic, CYP2C19 and CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal elimination is 15-25% with a half-life of 90 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Caution with CYP2C19 poor metabolizers
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Lansoprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
24 HR; SoluTab	No	Do not crush, chew, or open delayed release capsule or SoluTab	No	Aripiprazole, dexlansoprazole	No

Drug Interactions: Lansoprazole

Typical Agents	Mechanism	Clinical Management
Antacids	Increase gastric pH and prevent dissolution of lansoprazole granules, reducing bioavailability of lansoprazole	Administer lansoprazole at least 1 h after antacid therapy
Clopidogrel	May decrease the effect of clopidogrel on platelet inhibition, resulting in cardiovascular events (MI, stroke, death)	Avoid concurrent use; consider alternative acid-reducing agent such as H_2 inhibitor
CYP2C19 and CYP3A4/5 inducers	Increased metabolism of lansoprazole, decreased efficacy	Avoid concurrent use or increase dose of lansoprazole
CYP2C19 and CYP3A4/5 inhibitors	Decreased metabolism of lansoprazole and increased risk of lansoprazole toxicity	Avoid concurrent use or decrease dose of lansoprazole
pH-dependent drugs (erlotinib, mycophenolate, etc)	As lansoprazole lowers gastric pH, absorption of drugs that require acid environment is reduced	Avoid concurrent use

Adverse Reactions: Lansoprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, headache	Stevens-Johnson syndrome, rhabdomyolysis, acute interstitial nephritis, *Clostridium diff cle* diarrhea, hypomagnesemia

Efficacy Monitoring Parameters. Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

Toxicity Monitoring Parameters. Seek medical attention if severe headache or blistering skin rash occurs.

Key Patient Counseling Points. Should be taken on an empty stomach 1 h before eating. Should not be taken with antacids. For those unable to swallow capsules, capsules may be opened and sprinkled on 1 tablespoon of applesauce if intact granules swallowed immediately.

Clinical Pearls. Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; counsel patient to complete full regimen if prescribed for *H. pylori* management. Other PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of bone fracture with long-term use, use with caution in those with osteoporosis. Medication guide required at dispensing.

LATANOPROST: Xalatan, Various

Class: Prostaglandin, Antiglaucoma Agent

Dosage Forms. Ophthalmic Solution: 0.005%

Common FDA Label Indication, Dosing, and Titration.

1. Ocular hypertension, open-angle glaucoma: 1 drop in affected eye(s) daily in the evening

Off-Label Uses. None

MOA. Latanoprost is a prostaglandin F2-alpha analog. It is believed to reduce IOP by increasing the outflow of aqueous humor. Studies suggest that the main mechanism of action is increased uveoscleral outflow, but the exact mechanism is unknown.

Drug Characteristics: Latanoprost

Dose Adjustment Hepatic	Not required	**Absorption**	Absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active. Systemic absorption following ocular instillation is very low
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.16 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Metabolized within the cornea; any entering systemic circulation is metabolized in the liver, extent unknown
Pregnancy Category	C	**Elimination**	Renal elimination is 88-98% with a half-life of 17 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Pfizer 0.005% solution pictured

Medication Safety Issues: Latanoprost

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Lantus, Travatan, Xalacom	No

Drug Interactions: Latanoprost

Typical Agents	Mechanism	Clinical Management
Pilocarpine	Coadministration decreases access of latanoprost to the receptor and increases resistance to flow through the uveoscleral pathway	Bedtime dose of pilocarpine should be given at least 10 min (preferably 1 h) after latanoprost

Adverse Reactions: Latanoprost

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Blurred vision, itching, sensation of foreign body in eye, hyperpigmentation of eyelid, iris pigmentation	Dry eye, eyelid edema	Macular retinal edema, diplopia, keratitis

Efficacy Monitoring Parameters. Reduction in IOP.

Toxicity Monitoring Parameters. Seek medical attention if symptoms of ocular irritation are severe.

Key Patient Counseling Points. Wash hands and remove contact lenses before using the medicine. For administration, lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Put the cap on the bottle right away.

Clinical Pearls. If used concurrently with pilocarpine, separate dose by 1 h if possible. Separate administration from other ophthalmic products by at least 5 min. Advise patients that there is a risk of permanent increased iris pigmentation associated with instillation of this product. Do not administer more than once daily to avoid loss of therapeutic effect. Store intact bottles under refrigeration. Opened bottles may be stored at room temperature for 6 wk.

LEVALBUTEROL: Xopenex HFA

Class: Selective β_2-Agonist; Bronchodilator

Dosage Forms. Metered Dose Inhaler: 0.045 mg/actuation; **Nebulization Solution:** 0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/3 mL

Common FDA Label Indication, Dosing, and Titration.

1. Asthma, bronchospasm: Adults and Children ≥4 y of age, MDI, 2 inhalations q4-6h prn (*max* 2 inhalations q4h); by nebulizer, 0.63 mg TID (*max* 1.25 mg TID)

Off-Label Uses.

1. Asthma, acute exacerbation: Children ≥4 y of age, MDI, 4-8 inhalations q20min × 3 doses, then q1-4h prn; Adults, MDI, 4-8 inhalations po q20min up to 4 h, then q1-4h prn; by nebulizer, 1.25-2.5 mg q20min × 3 doses, then q1-4h prn

MOA. Activation of β_2-adrenergic receptors on airway smooth muscle leads to the activation of adenylate cyclase and to an increase in the intracellular concentration of cyclic-3′, 5′-adenosine monophosphate (cyclic AMP). The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Levalbuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles.

Sepracor pictured

Drug Characteristics: Levalbuterol

Dose Adjustment Hepatic	Not required	**Absorption**	F = 30% after oral administration
Dose Adjustment Renal	Not required	**Distribution**	After inhalation, Vd is ~1900 L
Dialyzable	Not dialyzable	**Metabolism**	Oral doses undergo rapid metabolism in the GI tract; hepatic metabolism of inhaled doses
Pregnancy Category	C	**Elimination**	Renal elimination is 80-100% with a half-life of 5-7 min
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Levalbuterol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
HFA	No	No	No	Xanax	No

Drug Interactions: Levalbuterol

Typical Agents	Mechanism	Clinical Management
Other short-acting sympathomimetics	May potentiate levalbuterol effect	Avoid concurrent use
Beta-blockers	May decrease effectiveness of levalbuterol and produce bronchospasm	Avoid use of nonselective beta-blockers in patients with asthma; monitor PFTs if cardioselective beta-blockers clinically indicated

Adverse Reactions: Levalbuterol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Vomiting	Chest pain, palpitations, tachyarrhythmia, tremor, pharyngitis, rhinitis	Paradoxical bronchospasm, anaphylaxis, cardiac dysrhythmias

Efficacy Monitoring Parameters. Resolution of asthma symptoms and improvement in PFTs.

Toxicity Monitoring Parameters. BP, HR.

Key Patient Counseling Points. Instruct patient on proper inhaler technique. Wash the mouthpiece and air dry thoroughly at least once a week (may cease to deliver medication if mouthpiece becomes blocked). Store the inhaler at room temperature, away from heat and direct light. Do not freeze. Do not keep this medicine inside a car where it could be exposed to extreme heat or cold. Contact prescriber if the need to use more levalbuterol to control symptoms than usual as this may indicate asthma deterioration.

Clinical Pearls. The National Heart, Lung and Blood Institute asthma guidelines recommend SABA as the drug of choice for treating acute asthma symptoms and exacerbations. SABA are not recommended for regularly scheduled, daily, long-term use.

LEVETIRACETAM: Keppra, Keppra XR, Various

Mylan generic
250 mg pictured

Mylan generic
500 mg pictured

Teva generic
1000 mg pictured

Class: Anticonvulsant

Dosage Forms. **Tablet:** 250 mg, 500 mg, 750 mg, 1000 mg; **Tablet, Extended Release:** 500 mg, 750 mg; **Oral Solution:** 100 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Myoclonic seizure, adjunct: Children ≥12 y of age and Adults, initial, 500 mg po bid, titrate to target dose of 3000 mg/d
2. Partial seizure, adjunct: Children ≥16 y of age and Adults, immediate release, initial, 500 mg po bid, *max* 3000 mg/d; extended release, initial, 1000 mg po qd, *max* 3000 mg/d; Children 4-15 y of age, immediate release, initial, 10 mg/kg po bid, *max* 60 mg/kg/d
3. Tonic-clonic seizure, primary generalized, adjunct: Children ≥16 y of age and Adults, initial, 500 mg po bid, titrate to target dose of 3000 mg/d; Children 6-15 y of age, initial, 10 mg/kg po bid, titrate to target dose of 60 mg/kg/d

Off-Label Uses. None

MOA. Levetiracetam is a pyrrolidine derivative that is structurally unrelated to other AEDs. Its mechanism of action is unclear and does not relate to any known mechanisms of neuronal excitation or inhibition. The action of levetiracetam in animal models of seizures and epilepsy is unique from other AEDs.

Drug Characteristics: Levetiracetam

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%; minor effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, reduce dose by 67%; CrCl = 30-50 mL/min, reduce dose by 50%	**Distribution**	<10% protein bound
Dialyzable	CrCl <30 mL/min, reduce dose by 67%; CrCl = 30-50 mL/min, reduce dose by 50%	**Metabolism**	Minimal and via hydrolysis
Pregnancy Category	C	**Elimination**	Renal elimination is 66% unchanged and 20-25% in feces, with a half-life of 6-8 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Levetiracetam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Keppra Keppra XR	LevETIRAcetam	Do not crush ER tablets	No	LevOCARNitine, levofoxacin	No

Drug Interactions: Levetiracetam

Typical Agents	Mechanism	Clinical Management
Carbamazepine	Increased risk of carbamazepine toxicity	Use caution with concomitant therapy; monitor for side effects

Adverse Reactions: Levetiracetam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Asthenia, fatigue, headache, somnolence, vomiting	Abnormal behavior, agitation, depression, diarrhea, dizziness, hostile behavior, irritability, loss of appetite, mood swings, nausea, nasopharyngitis, neck pain	Pancytopenia, hepatotoxicity, suicidal thoughts, suicide

Efficacy Monitoring Parameters. Reduction in the frequency and severity of seizures.

Toxicity Monitoring Parameters. Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior, WBC, LFTs.

Key Patient Counseling Points. Instruct patient to swallow extended-release tablet whole; do not chew, break, or crush. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report mood swings, agitation, hostile behavior, suicidal ideation, or unusual changes in behavior. Avoid sudden discontinuation of drug, may increase seizure activity.

Clinical Pearls. Safety and efficacy of tablets and solution not established in children <4 y of age. Safety and efficacy of extended-release tablet not established in children <16 y of age. Patients weighing <20 kg should be dosed with the oral solution. Data suggest an increased risk of suicidal behavior or ideation may exist in patients receiving therapy with AEDs. Pregnancy: up to a 50% dose increase during 3rd trimester with subsequent dose reduction after delivery may be necessary. Do not stop abruptly, increased risk of seizures. Dispense with medication safety guideline.

LEVOCETIRIZINE: Xyzal

Class: Antihistamine

Dosage Forms. **Oral Solution:** 2.5 mg/5 mL; **Oral Tablet:** 5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Idiopathic urticaria, perennial or seasonal allergic rhinitis: Children 6 mo to 5 y of age, 1.25 mg po daily; Children 6-11 y of age, 2.5 mg po daily; Children ≥12 y of age and Adults, 5 mg po daily; doses should be given in the evening

Sanofi-Aventis 5 mg pictured

Off-Label Uses. None

MOA. Levocetirizine, an enantiomer of cetirizine, is a low-sedating, long-acting H_1-receptor antagonist that is a metabolite of hydroxyzine. It competitively inhibits the interaction of histamine with H_1 receptors, thereby preventing the allergic response.

Drug Characteristics: Levocetirizine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 85%, limited effect of food on absorption
Dose Adjustment Renal	CrCl = 30-50 mL/min, 2.5 mg po every other day; CrCl = 10-29 mL/min, 2.5 mg po twice per wk; CrCl <10 mL/min, avoid	**Distribution**	Vd = 0.4 L/kg with 95% protein binding
Dialyzable	Not dialyzable	**Metabolism**	Hepatic metabolism, <14%
Pregnancy Category	B	**Elimination**	Renal elimination is 85% (80% unchanged) with a half-life of 7-8 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to cetirizine, levocetirizine, hydroxyzine, patients with CrCl <10 mL/min, children <12 y with any renal impairment, any patient on hemodialysis	**Black Box Warnings**	None

Medication Safety Issues: Levocetirizine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Cetirizine	No

Drug Interactions: Levocetirizine

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Possible increase in sedation effects	Use concurrently with caution

Adverse Reactions: Levocetirizine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea in children	Sedation, headache, dry mouth, fatigue, and nausea	Agitation, seizures

Efficacy Monitoring Parameters. Improvement in rhinitis or urticaria symptoms.

Toxicity Monitoring Parameters. Seek medical attention for signs of severe CNS toxicity; monitor SCr.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

Clinical Pearls. An expensive alternative to racemic version (cetirizine) which is available generically and over the counter. Limited evidence suggesting any advantage over racemic compound.

LEVOFLOXACIN: Levaquin, Various

Class: Fluoroquinolone Antibiotic

Dosage Forms. Oral Solution: 25 mg/mL; **Oral Tablet:** 250 mg, 500 mg, 750 mg

Ortho-McNeil-Janssen pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bacterial prostatitis, chronic: 500 mg po daily × 28 d
2. Bacterial sinusitis, acute: 750 mg po daily × 5 d
3. Bronchitis, chronic, acute bacterial exacerbation: 500 mg po daily × 7 d
4. Community acquired pneumonia: 500-750 mg po daily × 7-14 d
5. Infection of skin and/or subcutaneous tissue: (uncomplicated) 500 mg po daily × 7-14 d
6. Pyelonephritis, acute: 250 mg po daily × 10 d

Off-Label Uses.

1. Chlamydial infection: 500 mg po daily × 7 d
2. Traveler's diarrhea: 500 mg po daily × 1-3 d

MOA. Levofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase, an enzyme responsible for the unwinding of DNA for transcription and subsequent supercoiling of DNA for packaging into chromosomal subunits. It is highly active against aerobic, gram-negative bacilli.

Drug Characteristics: Levofloxacin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 99%, no food effect, take without regard to meals
Dose Adjustment Renal	CrCl 20-50 mL/min, reduce dose by 50%; CrCl 5-19 mL/min, extend interval to 48 h	**Distribution**	Bile, blister, CSF, gynecologic tissues, lung, prostate, synovial fluid, sputum, tonsils
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 87% with a half-life of 6-8 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ciprofloxacin or other quinolones; concomitant tizanidine administration	**Black Box Warnings**	Myasthenia gravis; tendon rupture

Medication Safety Issues: Levofloxacin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	LevETIRAcetam	No

Drug Interactions: Levofoxacin

Typical Agents	Mechanism	Clinical Management
Antidiabetics	Hypogycemic or hyperglycemic episodes, mechanism unknown	Caution with concurrent use, monitor plasma glucose and consider dose adjustments of antidiabetic agent
Aluminum, calcium, and calcium-fortified foods, didanosine, iron	Decreased absorption of fluoroquinolones caused by chelation	Separate administration by 2 h before or 6 h after
Class III antiarrhythmic agents or other agents that effect the QTc interval	Additive potential for QTc prolongation	Contraindicated
Corticosteroids	Increased risk if tendon rupture	Counsel patients to discontinue levofoxacin and seek medical attention if tendon pain or rupture
NSAIDs	Increased risk of seizures via inhibition of GABA resulting in CNS stimulation	Avoid NSAIDs if possible
Warfarin	Increased risk of bleeding	Increased monitoring of INR and warfarin adjustments

Adverse Reactions: Levofoxacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Photosensitivity	Nausea and vomiting, rash, myalgia, arthralgia, tendinitis, headache	Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac arrest, cardiac arrhythmias, liver failure, tendon rupture, psychosis, glucose abnormalities, *C. diffcile* colitis

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Baseline SCr.

Key Patient Counseling Points. Seek medical attention if decreased urination, yellowing of eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, or tendon pain. Take with or without food, but not with milk, yogurt, or other dairy products or calcium-fortified products (some juices and breads). If using antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc, take levofloxacin at least 2 h before or 6 h after these medicines.

Clinical Pearls. Not approved in children <18 y of age. Oral and IV dosing is interchangeable. Increased risk of tendon rupture in patients >60 y of age. Medication guide required at dispensing.

LEVOTHYROXINE: Synthroid, Various

Class: Thyroid Supplement

Dosage Forms. **Oral Tablet:** 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, 200 mcg, 300 mcg; **Oral Capsule:** 13 mcg, 25 mcg, 50 mcg, 75 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg

Mylan generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypothyroidism: Oral, maintenance, individualized based on clinical response and serum TSH levels; Adults, 25-300 mcg po daily; Infants 0-3 mo of age, 10-15 mcg/kg/d po daily, Infants 3-6 mo of age, 8-10 mcg/kg/d po daily, Infants 6-12 mo of age, 6-8 mcg/kg/d po daily, Children 1-5 y of age, 5-6 mcg/kg/d po daily, Children 6-12 y of age, 4-5 mcg/kg/d po daily, Children ≥12 y of age, growth and puberty incomplete) 2-3 mcg/kg/d po daily, Children ≥12 y of age, growth and puberty complete, 1.7 mcg/kg/d
2. Thyroid-stimulating hormone suppression, pituitary: Thyroid cancer, doses >2 mcg/kg/d po are usually required to suppress TSH <0.1 milliunits/L

Off-Label Uses.

1. Toxicity due to radiotherapy; use same age-based dosing as hypothyroidism

MOA. Levothyroxine sodium is a synthetic thyroid hormone. The endogenous thyroid hormones, T3 and T4, diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins.

Drug Characteristics: Levothyroxine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40-80%, increases with fasting
Dose Adjustment Renal	Not required	**Distribution**	Vd = 8.7-9.7 L; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Approximately 80% of levothyroxine sodium is deiodinated into T3 in the liver, kidney, and other tissues. It can also be metabolized by conjugation with glucuronides and sulfates and then enter into enterohepatic recirculation
Pregnancy Category	A	**Elimination**	Renal excretion is 50% with a half-life of 7 d
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, nontoxic diffuse goiter or nodular thyroid disease, thyrotoxicosis, acute MI, treatment of obesity or weight loss, uncorrected adrenal insufficiency; may precipitate acute adrenal crisis	**Black Box Warnings**	Not for weight reduction

Medication Safety Issues: Levothyroxine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	LamoTRIgine, Lanoxin, levofloxacin, liothyronine	No

Drug Interactions: Levothyroxine

Typical Agents	Mechanism	Clinical Management
Aluminum, calcium- and magnesium-containing antacids, iron, sucralfate, orlistat, etc	Decreased absorption of levothyroxine	Separate administration by 4 h
Estrogens	Estrogen-induced increases in serum thyroxine-binding globulin concentration	Monitor and consider increasing dose of levothyroxine
Eltrombopag	Inhibition of OATP1B1-mediated elimination of levothyroxine by eltrombopag	Monitor and consider decreasing dose of levothyroxine
Imatinib	Decreased levothyroxine effectiveness and worsening of hypothyroidism	Monitor and consider increasing dose of levothyroxine
Phenytoin, rifampin, simvastatin	Increased levothyroxine clearance	Monitor and consider increasing dose of levothyroxine
Warfarin	Enhanced anticoagulant effect	Monitor and consider warfarin dose adjustment

Adverse Reactions: Levothyroxine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Appetite decreased, anxiety, diarrhea, insomnia	Aggravation of preexisting cardiovascular disease, hyperthyroidism

Efficacy Monitoring Parameters. Serum TSH, T(3), and T(4) levels. T(3) normal range is 100-200 ng/dL. T(4) normal range is 4.5-11.2 mcg/dL. Free T4 normal range is 0.7-1.8 ng/dL. TSH level should be between 0.5 and 3.0 mIU/L in those treated for a thyroid disorder. Resolution of symptoms of hypothyroidism, fatigue, edema, hair loss, cold intolerance, and lethargy.

Toxicity Monitoring Parameters. Monitor patients with preexisting cardiovascular disease for exacerbation of symptoms.

Key Patient Counseling Points. May require 6-8 wk for symptomatic improvement. Avoid abrupt discontinuation. Take on an empty stomach, with water at least 30 min before food. Avoid antacids and iron within 4 h of dose.

Clinical Pearls. Not recommended for weight loss. May cause serious adverse effects and death in euthymic patients using it for weight loss.

LIDOCAINE TOPICAL PATCH: Lidoderm

Endo 5% patch pictured

Class: Local Anesthetic

Dosage Forms. Topical Patch: 5%

Common FDA Label Indication, Dosing, and Titration.

1. Postherpetic neuralgia and localized pain: 1-3 patches topically simultaneously for up to 12 h within a 24-h period

Off-Label Uses. None

MOA. Lidocaine is an amide-type local anesthetic agent and is suggested to stabilize neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses. The penetration of lidocaine in patch form into intact skin is sufficient to produce an analgesic effect, but less than the amount necessary to produce a complete sensory block.

Drug Characteristics: Lidocaine Topical Patch

Dose Adjustment Hepatic	Severe hepatic dysfunction, use fewer patches, for shorter periods of time, and/or with longer treatment-free intervals	**Absorption**	Only 3% of administered dose is absorbed systemically when applied to intact skin
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Yes	**Metabolism**	Not absorbed
Pregnancy Category	B	**Elimination**	Not absorbed
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Lidocaine Topical Patch

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Lidocaine Topical Patch. Minimal systemic absorption, none known.

Adverse Reactions: Lidocaine Topical Patch

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Skin irritation, somnolence	Hypotension, nausea, vomiting, confusion, dizziness, headache, paresthesia, constipation, tremor	Cardiac arrest, cardiac dysrhythmia, seizure, methemoglobinemia

Efficacy Monitoring Parameters. Relief from pain.

Toxicity Monitoring Parameters. Application of too many patches, for too long a period of time, and/or without adequate drug-free period may increase toxicity; application to broken skin or covering with occlusive dressing may lead to toxicity, particularly cardiac dysrhythmia.

Key Patient Counseling Points. Instruct patients on the appropriate application process. Leave patches on skin for no more than12 h within a 24-h period. Caution patients to administer only as directed, to intact skin, without covering with occlusive dressing or tight clothes.

Clinical Pearls. Patches may be cut into smaller sizes prior to removal of release liner to refine dose to meet patients' needs. Patients should be instructed to fold used patches after removal so that the adhesive side sticks to itself and safely discard used patches or pieces of cut patches where children and pets cannot get to them. Accidental ingestion of used patches can lead to serious adverse effects.

LINAGLIPTIN: Tradjenta

Class: Dipeptidyl peptidase IV inhibitor

Dosage Forms. Oral Tablet: 5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes, type 2: 5mg po daily

Off-Label Uses. None

MOA. Binds to and inhibits the dipeptidyl peptidase IV enzyme, resulting in prolonged incretin levels. Incretin hormones regulate glucose metabolism by increasing insulin secretion and release.

Drug Characteristics: Linagliptin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 30%
Dose Adjustment Renal	Not required	**Distribution**	Protein binding 70-80%
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate, P-glycoprotein substrate
Pregnancy Category	B	**Elimination**	80% in the feces unchanged. Half-life is 12 h, enzyme binding can persist >100 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Linagliptin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	No	No

Drug Interactions: Linagliptin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased linagliptin metabolism increases risk of linagliptin toxicity	Avoid strong CYP3A4/5 inhibitors, moderate inhibitors, monitor carefully and consider linagliptin dose reduction
CYP3A4/5 inducers	Increased linagliptin metabolism decreases linagliptin efficacy	Avoid strong CYP3A4/5 inducers, monitor carefully and consider linagliptin dose increases
P-glycoprotein inhibitors	Decreased linagliptin transport increases risk of linagliptin toxicity	Monitor carefully and consider linagliptin dose reduction
P-glycoprotein inducers	Increased linagliptin transport decreases linagliptin efficacy	Monitor carefully and consider linagliptin dose increases
Corticosteroids, thiazide diuretics	May decrease the hypoglycemic effect of linagliptin	Monitor and consider dose adjustments of linagliptin

Adverse Reactions: Linagliptin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypoglycemia	Headache, weight gain, diarrhea, arthralgia	Acute pancreatitis, anaphylaxis, angioedema, hypersensitivity

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%

Toxicity Monitoring Parameters. Severe abdominal pain, hypoglycemia

Key Patient Counseling Points. Monitor blood glucose frequently (2-4 times per day); if <70 mg/dL eat candy or juice and contact prescriber. Take with or without food, but at same time each day.

Clinical Pearls. Metformin is first-line therapy for type 2 diabetes and has been shown to be more effective than DPP-4 monotherapy. Linagliptin may be added as a 2nd agent in patients not controlled on metformin or as first-line therapy in patients with contraindications for metformin, such as renal dysfunction.

LIRAGLUTIDE: Victoza

Class: Glucagon-Like Peptide-1-Receptor Agonist

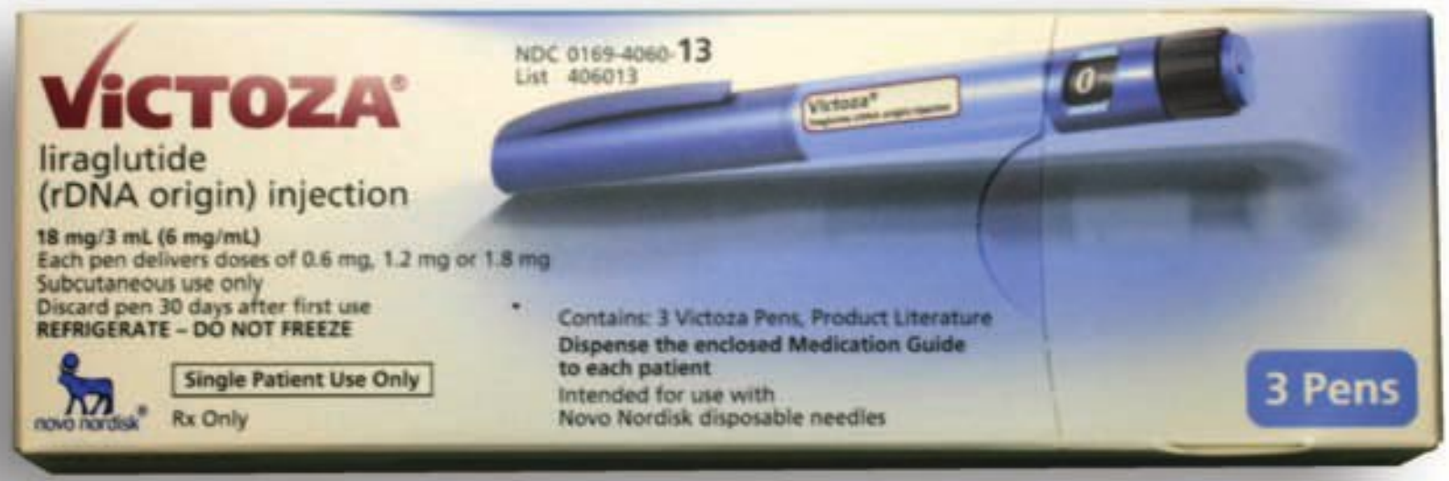
Dosage Forms. Solution, Pen Injector: 18 mg/3 mL

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes, type 2: 0.6 mg sq once daily for 1 wk, then increase to 1.2 mg sq once daily

Off-Label Uses. None

MOA. Analog of glucagon-like peptide-1, which increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, slows gastric emptying, and decreased food intake.



Drug Characteristics: Liraglutide

Dose Adjustment Hepatic	Use with caution in patients with severe hepatic dysfunction	**Absorption**	F = 55%
Dose Adjustment Renal	Use with caution in patients with severe renal dysfunction	**Distribution**	Vd = 13L, protein binding >98%
Dialyzable	Unknown	**Metabolism**	Metabolized by dipeptidyl peptidase IV
Pregnancy Category	C	**Elimination**	5% in the feces, 6% in urine, Half-life is 13 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, multiple endocrine neoplasia syndrome type 2, history or family history of medullary thyroid carcinoma	**Black Box Warnings**	Increased risk of thyroid cancer

Medication Safety Issues: Liraglutide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	No	No

Drug Interactions: Liraglutide

Typical Agents	Mechanism	Clinical Management
Corticosteroids, thiazide diuretics	May decrease the hypoglycemic effect of liraglutide	Monitor and consider dose adjustments of liraglutide

Adverse Reactions: Liraglutide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, diarrhea, vomiting	Headache, hyperbilirubinemia, antibody development, injection site reactions	Acute renal failure, thyroid carcinoma, exacerbation of chronic renal failure, hypoglycemia, pancreatitis, hypersensitivity

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%

Toxicity Monitoring Parameters. Severe abdominal pain, SCr, LFTs

Key Patient Counseling Points. Monitor blood glucose frequently (2-4 times per day); if <70 mg/dL eat candy or juice and contact prescriber. Administer in upper arm, thigh, or abdomen. Change needle for each injection, do not share pens, even if needle is changed. If also using insulin, administer with separate injection in a non-adjacent area. Can be injected without regard to meals.

Clinical Pearls. Metformin is first-line therapy for type 2 diabetes. Liraglutide may be added as a 2nd agent in patients not controlled on metformin. An advantage of liraglutide over other therapies is lack of weight gain and no hypoglycemia.

LISDEXAMFETAMINE: Vyvanse

Class: Amphetamine, CNS Stimulant. C-II

Dosage Forms. Oral Capsule: 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg

Common FDA Label Indication, Dosing, and Titration.

1. Attention-deficit hyperactivity disorder (ADHD): 30 mg po daily in the morning, may titrate in 10-20 mg/d increments at weekly intervals to *max* dose of 70 mg po daily; discontinue if improvement not observed after 1 mo of dosage titration.

30 mg 40 mg 50 mg 60 mg

Shire generic pictured

Off-Label Uses. None

MOA. Lisdexamfetamine is converted to dextroamphetamine. The mechanism of action of dextroamphetamine in the treatment of ADHD is unknown. Amphetamines may block the reuptake of norepinephrine and dopamine at the presynaptic neuron and thus increase the release of norepinephrine and dopamine into the extraneuronal space.

Drug Characteristics: Lisdexamphetamine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3.5-4.6 L/kg; 60% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive metabolism in the blood by hydrolytic activity of red blood cells to dextroamphetamine and l -lysine
Pregnancy Category	C	**Elimination**	Renal elimination is 96% and 0.3% in feces, with a half-life of <1 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity/idiosyncrasy to sympathomimetic amines; MAOIs; symptomatic cardiovascular disease or advanced arteriosclerosis; moderate-severe hypertension; hyperthyroidism; glaucoma; agitated states; history of drug dependence	**Black Box Warnings**	Risk of abuse, misuse, diversion

Medication Safety Issues: Lisdexamphetamine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew capsule, but may be opened and dissolved in water	No	Visanne, ViVAXIM	No

Drug Interactions: Lisdexamphetamine

Typical Agents	Mechanism	Clinical Management
Tricyclic antidepressants	Increased risk of hypertension, other cardiac effects, and CNS stimulation	Use caution with concomitant therapy; monitor BP and for side effects
MAOIs	Increased risk of hypertensive crisis (headache, hyperpyrexia, hypertension)	Concomitant use contraindicated

Adverse Reactions: Lisdexamphetamine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dystonia, insomnia, hallucinations, irritability, loss of appetite, upper abdominal pain, xerostomia	Agitation, anxiety, decreased growth and development, diarrhea, dizziness, headache, increased BP, increased HR, nausea, rash, vomiting, weight loss	Chest pain, new onset or worsening of existing psychotic disorders, stroke, sudden cardiac death, tachycardia

Efficacy Monitoring Parameters. Improvement of mental and behavioral symptoms of ADHD (inappropriate inattention, impulsivity, hyperactivity, and cognitive performance).

Toxicity Monitoring Parameters. Palpitations, near syncope, or syncope; may be indicative of a cardiac condition. BP and HR should be evaluated at baseline, during routine follow-up within 1-3 mo, and at follow-up visits every 6-12 mo.

Key Patient Counseling Points. Take dose in the morning with or without food. Growth rate and weight may need to be monitored more frequently for children using this drug. Report new or worsened psychiatric problems (behavior and thought problems, bipolar illness, aggressive behavior or hostility). Also report chest pain, palpitations, dyspnea, or signs/symptoms of cardiac dysrhythmia, myocardial infarction, or cerebrovascular accident. Capsule may be opened and the entire contents dissolved in a glass of water, stirring until dispersed completely and consuming entire mixture immediately.

Clinical Pearls. Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and must be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events. A complete family and patient history for conditions associated with sudden cardiac death is required and current use of any other prescription or over-the-counter medications needs to be determined. A complete physical evaluation of the patient for hypertension, cardiac murmurs, physical findings associated with Marfan syndrome, and signs of irregular cardiac rhythms should be conducted. Medication guide required at dispensing.

LISINOPRIL: Prinivil, Zestril, Various

Class: ACE-I, Antihypertensive

Dosage Forms. **Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Acute myocardial infarction: 5-10 mg po daily × 6 wk
2. Heart failure: 2.5-5 mg po daily, may titrate to 40 mg/d
3. Hypertension: Adults, 10 mg po daily, may titrate to 80 mg/d; Children 6-16 y of age, 0.07 mg/kg (*max* 5 mg/d) po daily, may titrate to 0.61 mg/kg/d (*max* 40 mg/d)

Off-Label Uses. None

MOA. Lisinopril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.

Drug Characteristics: Lisinopril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 25% (F = 16% in heart failure), no effect of food on absorption
Dose Adjustment Renal	CrCl 10-30 mL/min: initial dose 5 mg/d; CrCl <10 mL/min: initial dose is 2.5 mg/d; dialysis patients: initial dose is 2.5 mg/d, supplemental dose equivalent to 20% of daily dose after hemodialysis	**Distribution**	25% protein bound
Dialyzable	Yes (hemodialysis and peritoneal)	**Metabolism**	Not metabolized
Pregnancy Category	C (1st trimester), D (2nd and 3rd trimesters)	**Elimination**	Renal elimination is 50-70% with a half-life of 12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to lisinopril or other ACE-Is, history of ACE-I-induced angioedema, and hereditary or idiopathic angioedema, concurrent use with aliskerin in diabetic patients	**Black Box Warnings**	Pregnancy

Teva generic pictured

Medication Safety Issues: Lisinopril

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Fosinopril, Lioresal, ZyPREXA, RisperDAL	No

Drug Interactions: Lisinopril

Typical Agents	Mechanism	Clinical Management
Angiotensin-receptor blockers, potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use, or monitor for anemia or leukopenia
Cyclosporine	Increased risk of nephrotoxicity	Avoid concurrent use or monitor SCr levels
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly
NSAIDs	Decreased antihypertensive and natriuretic effect of lisinopril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr
Potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels

Adverse Reactions: Lisinopril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, dizziness, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting	Angioedema, birth defects, liver failure

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, and urine protein.

Key Patient Counseling Points. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

Clinical Pearls. Observe patients who are volume depleted for at least 2 h after taking the initial dose of lisinopril. As effective as atenolol in the treatment of hypertension. Recommended as first line therapy with HCTZ for HTN.

LITHIUM CARBONATE: Eskalith, Eskalith-CR, Lithobid, Various

Class: Antimanic

Dosage Forms. **Oral Capsule:** 150 mg, 300 mg, 600 mg; **Oral Tablet:** 300 mg; **Oral Tablet, Extended Release:** 300 mg, 450 mg; **Oral Solution**: 300 mg/5 mL (as a citrate)

Roxane generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disorder, maintenance therapy: Adults and Children >12 y of age, extended release, 900-1800 mg/d po in 2-3 divided doses; immediate release, initial 300 mg po daily, may titrate to 900-1800 mg po in 3-4 divided doses
2. Bipolar disorder, manic episode: Adults and Children >12 y of age, extended release, 1800 mg/d po in 2-3 divided doses; immediate release, 600 mg po tid

Off-Label Uses.

1. Depression: Adults and Children >12 y of age, extended release, 600-1200 mg/d po in 2-3 divided doses; immediate release, 300 mg po bid-qid

MOA. Lithium's mechanism of anti-manic effect is unknown; it alters the actions of several second-messenger systems (eg, adenylate cyclase and phosphoinositol). Alters cation transport across cell membrane in nerve and muscle cells and influences reuptake of serotonin and/or norepinephrine; second-messenger systems involving the phosphatidylinositol cycle are inhibited

Drug Characteristics: Lithium

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90-100%, food has no effect on absorption
Dose Adjustment Renal	CrCl 10-50 mL/min, give 50-75% of the usual dose; CrCL <10 mL/min, give 25-50% of usual dose at the normal dosing interval	**Distribution**	Vd = 1.4 L/kg, no protein binding
Dialyzable	Yes, a maintenance dose should be given following hemodialysis	**Metabolism**	Not metabolized
Pregnancy Category	D	**Elimination**	Renal elimination is 89-98% and <1% fecal elimination, with a half-life of 14-24 h (up to 2.43 d with long-term therapy)
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Severe debilitation, dehydration, or sodium depletion; significant cardiovascular disease; significant renal impairment; concomitant diuretic therapy	**Black Box Warnings**	Lithium levels required

Medication Safety Issues: Lithium

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CR	No	Do not chew or crush ER formulations	No	Estratest	No

Drug Interactions: Lithium

Typical Agents	Mechanism	Clinical Management
Acetazolamide, sodium bicarbonate	Decreased lithium concentrations and effectiveness	Monitor lithium efficacy and serum concentrations
ACE-Is, ARBs, diuretics	Increased risk of lithium toxicity and/or nephrotoxicity	Avoid concomitant use of ACI-Is and ARBs; diuretics are contraindicated
Agents that prolong QT interval	Additive cardiotoxicity	Avoid concurrent use or monitor ECGs
Antipsychotic drugs, clozapine	Increased risk of adverse effects and extrapyramidal symptoms	Monitor for adverse effects
MAOIs	Increased risk of malignant hyperpyrexia	Avoid concomitant use; allow 2 wk to elapse between discontinuation of MAOIs and initiation of lithium
SSRIs, linezolid	Increased lithium concentrations and/or an increased risk of serotonin syndrome	Monitor for adverse effects and lithium serum concentrations

Adverse Reactions: Lithium

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Cardiac dysrhythmias, fine tremor, hypothyroidism, leukocytosis, thrombocytosis, xerostomia	Ataxia, blurred vision, diarrhea, EEG changes, ECG changes, headache, muscle weakness, nausea, oliguria, polyuria, somnolence, tinnitus, vomiting	Hypotension, nephrotoxicity, seizure, hypercalcemia, hyperparathyroidism

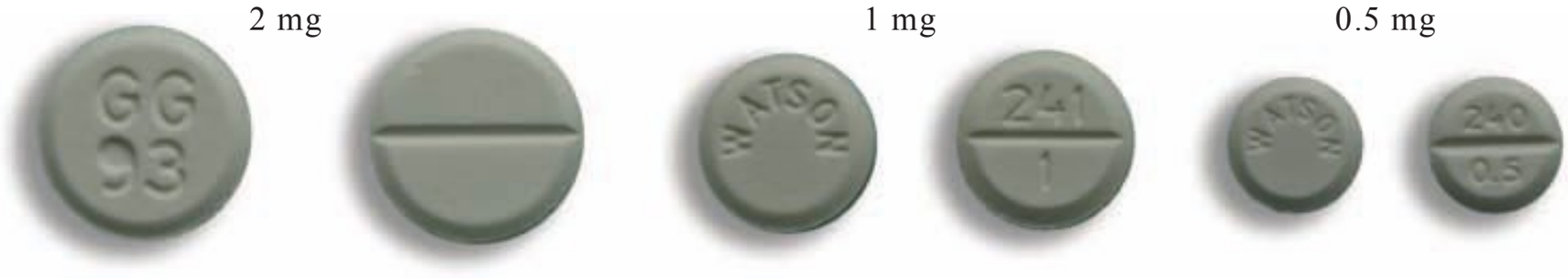
Efficacy Monitoring Parameters. Reduction in manic symptoms, prevention of manic and depressive episodes. Drug levels: between 1 and 1.5 mEq/L for acute mania and 0.6 and 1.2 mEq/L for long-term control; serum concentrations should not exceed 2.0 mEq/L during acute therapy. Drug levels should be drawn just prior to the next dose.

Toxicity Monitoring Parameters. Kidney and thyroid function, hydration status, sodium levels. Periodic EEG and ECG exams if medically warranted.

Key Patient Counseling Points. Swallow extended-release tablets whole; do not crush or chew. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report signs/symptoms of toxicity, which may vary depending on the degree of toxicity. These may include diarrhea, vomiting, tremor, ataxia, drowsiness, muscle weakness, lack of coordination, giddiness, blurred vision, tinnitus, or large volumes of dilute urine. Maintain adequate fluid intake and normal salt intake.

Clinical Pearls. Safety and effectiveness in patients <12 y of age have not been established. Lithium toxicity is closely related to serum lithium levels and can occur at doses close to therapeutic levels. Ability to tolerate lithium is greater during the acute manic phase and decreases when manic symptoms subside. Do not confuse dosing in mEq versus mg. Doses should be in mg (300 mg = 8 mEq).

LORAZEPAM: Ativan, Various



Sandoz generic pictured

Watson generic pictured

Class: Benzodiazepine, Short or Intermediate Acting. C-IV

Dosage Forms. **Oral Tablet:** 0.5 mg, 1 mg, 2 mg; **Oral Solution:** 2 mg/mL, 4 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Anxiety: Adults, 1 mg po bid-tid
2. Insomnia, due to anxiety or situational stress: Adults and Children >12 y of age, 2-4 mg po hs

Off-Label Uses

1. Alcohol withdrawal syndrome: Initial, 2 mg po qid, then 1 mg qid × 8 doses

MOA. Enhance the postsynaptic effect of the inhibitory neurotransmitter, GABA.

Drug Characteristics: Lorazepam

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90-93%, no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.3 L/kg; 85% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensively metabolized via glucuronidation
Pregnancy Category	D	**Elimination**	Renal elimination is 88% with a half-life of 12 h in adults; increased half-life in other age groups
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to benzodiaz-epines, narrow-angle glaucoma	**Black Box Warnings**	None

Medication Safety Issues: Lorazepam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Intensol	LORazepam	No	No	ALPRAZolam, clonazePAM	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium

Drug Interactions: Lorazepam

Typical Agents	Mechanism	Clinical Management
Alfentanil, opioids, and other respiratory depressants	Additive respiratory depression	Avoid if possible and consider dose reductions of both agents
Amitriptyline	Additive psychomotor defects	Monitor and advise patient
Ethinyl estradiol and other estrogen-based birth control products	Increased lorazepam metabolism and decreased effectiveness	May require higher dose of lorazepam
Valproic acid	Decreased metabolism of lorazepam	Reduce lorazepam dose by 50%

Adverse Reactions: Lorazepam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Drowsiness, impaired motor coordination, retrograde amnesia	Asthenia, dizziness, blurred vision, depression	Seizures, mania, depression, withdrawal symptoms

Efficacy Monitoring Parameters. Reduction in anxiety symptoms, alcohol withdrawal symptoms (BP, tremor), onset of sleep.

Toxicity Monitoring Parameters. Seek medical attention if severe drowsiness, thoughts of suicide, or seizures; monitor BP, HR.

Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

Clinical Pearls. May be benzodiazepine of choice in impaired liver function and for nursing mothers. Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Avoid abrupt discontinuation after chronic use, may cause seizures. Safety not established for children <12 y of age.

LOSARTAN: Cozaar, Various

Class: Angiotensin II Receptor Antagonist, Antihypertensive

Dosage Forms. **Oral Tablet:** 25 mg, 50 mg, 100 mg

Merck 100 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, initial 50 mg po daily, may titrate to 25-100 mg po daily or bid; Children ≥6 y of age, 0.7 mg/kg po daily, *max* 50 mg po daily
2. Heart failure: Initial, 12.5 mg po daily, maintenance 50 mg po daily
3. Reduce risk of cerebrovascular accident, in hypertensive patients with left ventricular hypertrophy; prophylaxis, diabetic nephropathy: Initial, 50 mg po daily, may titrate to 100 mg podaily
4. Diabetic nephropathy: Initial, 50 mg daily, may titrate based on BP up to 100 mg po daily

Off-Label Uses.

1. Cardiovascular event risk, reduction: Adults, 50-100 mg po daily
2. Isolated systolic hypertension, left ventricular hypertension, nondiabetic kidney disease: 50 mg po daily

MOA. Losartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1), which is responsible for the physiologic effects of angiotensin II including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.

Drug Characteristics: Losartan

Dose Adjustment Hepatic	Starting dose, 25 mg po daily, *max* 100 mg/d	**Absorption**	F = 33%, food slows absorption and decreases Cmax by 10%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 34 L; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	14% hepatic, CYP2C9 and CYP3A4/5 substrate
Pregnancy Category	C (1st trimester), D (2nd and 3rd trimesters)	**Elimination**	Renal elimination is 35% and fecal elimination is 60% with a half-life 2 h (6-9 h for active metabolite, 5-carboxylic acid)
Lactation	Not recommended	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to losartan or other angiotensin II receptor antagonists, pregnancy	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Losartan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Colace, Coreg	No

Drug Interactions: Losartan

Typical Agents	Mechanism	Clinical Management
ACE-Is, potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Aliskiren	Increased risk of hyperkalemia	Monitor serum potassium level
CYP2C9 and CYP3A4/5 inhibitors	Decreased losartan metabolism and increased risk of losartan toxicity	Monitor BP; consider dose reductions of losartan
CYP2C9 and CYP3A4/5 inducers	Increased losartan metabolism and decreased losartan efficacy	Monitor BP; consider dose increases of losartan
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly
Potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium level
Nonsteroidal anti-inf ammatory drugs	Decreased antihypertensive and natriuretic effect of losartan, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels

Adverse Reactions: Losartan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Anorexia, back pain, constipation, dizziness, dyspepsia, hypotension, hyperkalemia, leg pain, muscle cramps, myalgia, nausea, nephrotoxicity, rash, tachycardia	Angioedema, birth defects, hepatotoxicity, rhabdomyolysis

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema. Baseline and periodic electrolyte panel, renal function tests, and urine protein are recommended.

Key Patient Counseling Points. Avoid pregnancy. Avoid sudden discontinuation; rebound hypertension can occur. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek medical attention if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs.

Clinical Pearls. Observe patients who are volume depleted for at least 2 h after taking the initial dose and consider a lower starting dose.

LOTEPREDNOL: Alrex, Lotemax

Class: Corticosteroid, Ophthalmic

Dosage Forms. **Suspension, Ophthalmic:** 0.2%, 0.5%; **Ointment, Ophthalmic:** 0.5%; **Gel, Ophthalmic:** 0.5%

Common FDA Label Indication, Dosing, and Titration.

1. Temporary relief of seasonal allergic conjunctivitis: Instill 1 drop of 0.2% suspension qid
2. Inflammatory conditions: Instill 1-2 drops of 0.5% suspension in conjunctival sac of affected eye qid
3. Postoperative inflammation: Apply 1/2 inch of gel or 1-2 drops of 0.5% gel or suspension into conjunctival sac of affected eye qid continuing 24 h before surgery and for 2 wk after surgery

Off-Label Uses. None

MOA. Corticosteroids inhibit the inflammatory response including edema, capillary dilation, leukocyte migration, and scar formation

Drug Characteristics: Loteprednol

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, active eye infection	**Black Box Warnings**	None

Medication Safety Issues: Loteprednol

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Loteprednol: None known

Adverse Reactions: Loteprednol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, burning on instillation, discharge, dry eyes, itching, photophobia, abnormal vision/blurring	Irritation, corneal abnormalities, eyelid erythema, increased IOP	Cataract formation, changes in visual acuity, optic nerve damage, secondary eye infection

Efficacy Monitoring Parameters. Relief or prevention of redness, irritation and other inflammatory symptoms

Toxicity Monitoring Parameters. Assess for increased IOP if >10 d of treatment, signs and symptoms of infection

Key Patient Counseling Points. Suspension: Shake well before use. Take out contact before use, may put contacts back in 10 min after using suspension. Tilt head and drop into eye. Keep eyes closed after use and put pressure on inside corner of the eye. Ointment: Do not use contacts while using this product. To administer, gently pull down lower lid, and squeeze in gel. Let go of eyelid, but keep eye closed for 1-2 min. Gel: Turn upside down and shake once. Do not use contacts while using this product. Tilt head and drop into eye. Keep eyes closed after use and put pressure on inside corner of the eye. If using for both eyes, do not use same bottle in both eyes.

Clinical Pearls. Patients with allergic conjunctivitis should be advised to avoid triggers, rubbing their eyes, and reduce contact use. Cool compresses and refrigerated artificial tears can also reduce redness and irritation.

LOVASTATIN: Altoprev, Mevacor, Various

Class: HMG-CoA Reductase Inhibitor

Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg; **Oral Tablet, Extended Release:** 20 mg, 40 mg, 60 mg

Common FDA Label Indication, Dosing, and Titration.

1. Coronary arteriosclerosis, hypercholesterolemia, primary and mixed: Initial, 20 mg po daily, maintenance 10-80 mg po daily or in 2 divided doses; *max* 80 mg/d; Extended-release tablet: 20-60 mg po qhs
2. Familial hypercholesterolemia, heterozygous: Children 10-17 y of age, initial, 10 po daily, maintenance 10-40 mg po daily; *max* 40 mg/d

Sandoz generic pictured

Off-Label Uses. None

MOA. HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis.

Drug Characteristics: Lovastatin

Dose Adjustment Hepatic	Active liver disease or unexplained persistent elevation of liver enzymes, avoid use	**Absorption**	F = <5% with immediate release, improved to 30% with ER, food decreases absorption
Dose Adjustment Renal	CrCl <30mL/min, use caution if giving doses >20 mg/d	**Distribution**	>95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	80-85% hepatic, CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Renal elimination is <10% with a half-life of 2 h
Lactation	Contraindicated	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to lovastatin, active liver disease, pregnancy and lactation, concomitant use with HIV protease inhibitors, and unexplained persistent elevation of liver enzymes	**Black Box Warnings**	None

Medication Safety Issues: Lovastatin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush or chew ER formulations	No	AtorvaSTATin	No

Drug Interactions: Lovastatin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased lovastatin metabolism increase risk of lovastatin toxicity	Avoid concurrent use or monitor for myopathy and measure creatine kinase levels, *max* dose of lovastatin 20 mg/d for strong inhibitors (40 mg/d with verapamil, a moderate inhibitor). Protease inhibitors are contraindicated
CYP3A4/5 inducers	Increased lovastatin metabolism decreases lovastatin efficacy	Avoid concurrent use, or monitor lipids and consider dose increases of lovastatin
Fibrates, niacin	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use or monitor for myopathy and measure creatine kinase levels. Use lower doses of statins

Adverse Reactions: Lovastatin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myalgia, nausea, rash, hyperglycemia	Rhabdomyolysis, hepatotoxicity, increased risk of diabetes

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL-cholesterol, and triglyceride levels; increase in HDL-cholesterol levels. Assess at baseline and periodically during treatment.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity. LFTs, blood glucose, and HbA_{1c} should be performed at baseline, 6-12 wk after initiation of therapy, and periodically thereafter. Serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

Key Patient Counseling Points. Immediate-release tablets should be taken with the evening meal. Extended-release tablets should be taken at bedtime. Swallow extended-release tablets whole; do not chew, crush, or cut. Avoid alcohol, grapefruit, and grapefruit juice. Report signs/symptoms of rhabdomyolysis, jaundice (yellowing of skin or eyes), or renal failure. There are multiple significant drug-drug interactions with lovastatin. Consult a health-care professional prior to starting any new prescription or OTC medications. Lovastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

Clinical Pearls. Safety and efficacy of extended-release tablets not established in pediatric patients. Use increases risk of diabetes, especially in the elderly.

LUBIPROSTONE: Amitiza

Class: Chloride Channel Activator

Dosage Forms. Oral Capsule: 8 mcg, 24 mcg

Common FDA Label Indication, Dosing, and Titration.

1. Chronic idiopathic constipation: 24 mcg po bid
2. Irritable bowel syndrome with constipation: Females >18 y of age, 8 mcg po bid
3. Opioid induced constipation: 24 mcg po bid

Off-Label Uses. None

MOA. Lubiprostone is a bicyclic fatty acid that acts at the apical portion of the intestine as a chloride channel activator, which increases intestinal fluid secretion. When used for opioid-induced constipation activation of the chloride channel bypasses the antisecretory effects of opioids

Drug Characteristics: Lubiprostone

Dose Adjustment Hepatic	Moderate, reduce dose to 16 mcg bid; Severe, reduce dose to 8 mcg bid	**Absorption**	Poorly absorbed
Dose Adjustment Renal	Not required	**Distribution**	>94% protein bound
Dialyzable	Unknown	**Metabolism**	Rapid and extensive in stomach and jejunum by carbonyl reductase to active metabolite
Pregnancy Category	C	**Elimination**	Half-life of 0.9 -1.4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, bowel obstruction	**Black Box Warnings**	None

Medication Safety Issues: Lubiprostone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not crush or chew	No	No	No

Drug Interactions: Lubiprostone

Typical Agents	Mechanism	Clinical Management
Methadone	May decreases lubiprostone activation of chloride channels resulting in decreased lubiprostone efficacy	Monitor therapy and consider alternative constipation treatments

Adverse Reactions: Lubiprostone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache, nausea, diarrhea	Edema, dizziness, dyspnea, fatigue, abdominal pain, f atulence, vomiting, xerostomia	Anorexia, GERD, tachycardia

Efficacy Monitoring Parameters. Relief of constipation.

Toxicity Monitoring Parameters. Baseline LFTs, physical exam and history to rule out bowel obstruction.

Key Patient Counseling Points. Take with food and water to reduce risk of nausea. Seek medical attention chest pain, shortness of breath or severe GI symptoms. Dyspnea, described as chest tightness, has been reported and generally occurs with the 1st dose and resolves after a few hours without intervention.

Clinical Pearls. Not approved for males with irritable bowel syndrome, despite what you may see advertised directly to consumers.

MARAVIROC: Selzentry

Class: Antiretroviral Agent, CCR5 Antagonist

Dosage Forms. Oral Tablet: 150 mg, 300 mg

Common FDA Label Indication, Dosing, and Titration.

1. Treatment of CCR5-tropic HIV-1 infection, in combination with other antiretroviral agents: Adults, 300 mg po bid

Off-Label Uses. None

MOA. Selectively and reversibly binds to the chemokine (C-C motif receptor 5 [CCR5]) coreceptors located on human CD4 cells. CCR5 antagonism prevents interaction between the human CCR5 coreceptor and the gp120 subunit of the viral envelope glycoprotein, thereby inhibiting gp120 conformational change required for CCR5-tropic HIV-1 fusion with the CD4 cell and subsequent cell entry.

Viir Healthcare pictured

Drug Characteristics: Maraviroc

Dose Adjustment Hepatic	Use with caution if moderate or severe hepatic impairment	**Absorption**	F = 23-33%, food decreases absorption by 30-60%
Dose Adjustment Renal	Reduce dose to 150 mg bid if CrCl <30 mL/min; avoid if on interacting meds	**Distribution**	CSF
Dialyzable	No	**Metabolism**	Hepatic, CYP3A4/5 and ABCB1 major substrate
Pregnancy Category	B	**Elimination**	20% unchanged in feces, 14-34% renally eliminated as parent, half-life 14-18 h
Lactation	Weight risks and benefits	**Pharmacogenetics**	Requires trophism test for the presence of CCR5 on patient CD4 cells
Contraindications	Patients with CrCl <30 mL/min or ESRD who are taking potent CYP3A4/5 inhibitors or inducers	**Black Box Warnings**	Hepatotoxicity

Medication Safety Issues: Maraviroc

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Yes	Yes	No	No

Drug Interactions: Maraviroc

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased maraviroc metabolism and increased risk of maraviroc toxicity	Reduce dose of maraviroc to 150 mg bid if strong CYP3A5/5 inhibitor, monitor and consider dose reduction with moderate CYP3A4/5 inhibitors
CYP3A4/5 inducers	Increased maraviroc metabolism and decreased maraviroc efficacy	Increase dose of maraviroc to 600 mg bid with strong inducers

Adverse Reactions: Maraviroc

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Fever, rash, cough	Hypertension, insomnia, anxiety, fatigue, benign skin neoplasms, neutropenia, elevated LFTs, constipation, herpes infection	Coronary artery disease, angina, jaundice, hepatic failure, seizures

Efficacy Monitoring Parameters. HIV viral load, CD4 count, tropism assay, HIV resistance testing.

Toxicity Monitoring Parameters. LFTs, bilirubin.

Key Patient Counseling Points. Take with or without food. Do not chew or crush tablet. Does not prevent transmission of HIV, practice safe sex, do not share needles, etc. May cause drowsiness, avoid driving and concurrent CNS depressants.

Clinical Pearls. Not recommended for children <16 y of age. HIV may enter the cell via CCR5, CXCR4, or both receptors (called dual or mixed). Maraviroc is only indicated for HIV viruses that only use CCR5 for cell entry. Does not cure HIV. Medication guide required at dispensing.

MEASLES, MUMPS, RUBELLA VACCINE, LIVE: MMR-II

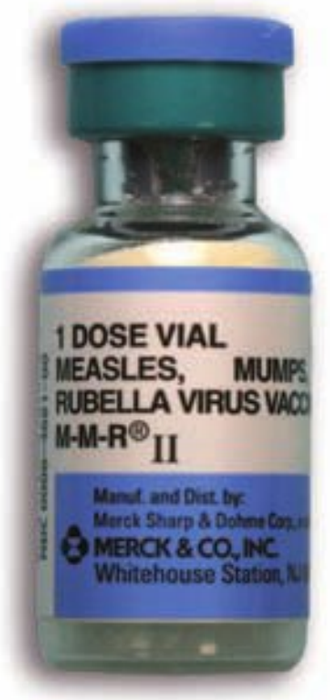
Class: Vaccine

Dosage Forms. **Lyophilized Powder for Subcutaneous Injection:** 0.5 mL after reconstitution with supplied diluent; also available in combination with varicella vaccine

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of measles, mumps, and rubella infections: Adults, 1 dose (2nd dose indicated for adults who are at high risk); Children, 1 dose at age 12 mo with a 2nd dose at age 4-6 y, prior to entering school

Off-Label Uses. None



Merck pictured

Drug Characteristics: Measles, Mumps, Rubella Vaccine, Live

Pregnancy Category	C	**ADME**	None known
Lactation	Generally considered safe during lactation	**Pharmacogenetics**	Not yet clinically relevant
Contraindications	Hypersensitivity to MMR vaccine or a component of the vaccine (egg, gelatin, neomycin); immunosuppression; pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Measles, Mumps, Rubella Vaccine, Live

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
MMR-II, MMRV	No	No	No	None	No

Drug Interactions: Measles, Mumps, Rubella Vaccine, Live

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression reduces vaccine efficacy and patients are at increased risk of measles infection	Delay MMR vaccine administration until corticosteroid therapy has been discontinued
Immunosuppressing agents	Immunosuppression reduces vaccine efficacy and patients are at increased risk of measles infection	Delay MMR vaccine administration until immunosuppressive therapy has been discontinued
Immune globulin or blood products	Interference with immune response to live vaccines	Delay MMR vaccine administration for a period of time depending on type and dose of immune globulin or blood product

Adverse Reactions: Measles, Mumps, Rubella Vaccine, Live

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Fever, arthralgia (adult females)	Rash	Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome, febrile seizure

Efficacy Monitoring Parameters. Prevention of measles, mumps, and rubella infections; although antibody concentrations might be measured, routine measurement for vaccine response is not recommended.

Toxicity Monitoring Parameters. Monitor for syncope after administration.

Key Patient Counseling Points. Some children may experience mild fever and rash 7-10 d after vaccine administration. Avoid pregnancy for 28 d following vaccine administration.

Clinical Pearls. Individuals born before 1957 can be considered immune unless a female of childbearing potential. Administer to females found to be seronegative to rubella following completion of pregnancy. If not administered simultaneously, MMR must be separated by at least 4 wk from other live vaccines. Ensure that international travelers are appropriately immunized. Avoid confusion with MMRV, which also contains varicella vaccine. Administer 2nd dose at least 28 d after 1st dose.

MECLIZINE: Antivert, Dramamine, Various

Class: Antihistamine, Antiemetic

Dosage Forms. Oral Tablet: 12.5 mg, 25 mg, 32 mg; **Oral Tablet, Chewable:** 25 mg

Common FDA Label Indication, Dosing, and Titration.

1. Motion sickness: 25-50 mg po 1 h before departure, may repeat q24h prn
2. Vertigo: 25-100 mg po daily in 1-3 divided doses, depending on clinical response

Off-Label Uses. None

MOA. Meclizine is an antihistamine that suppresses the vasodepressor response to histamine while only slightly inhibiting acetylcholine.

Rugby generic 25 mg pictured

Drug Characteristics: Meclizine

Dose Adjustment Hepatic	Not required	**Absorption**	Not known
Dose Adjustment Renal	Not required	**Distribution**	Vd = 7 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, minor CYP2D6 substrate
Pregnancy Category	B	**Elimination**	Excreted in urine and feces, half-life of 6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Meclizine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Anzemet, Axert	No

Drug Interactions: Meclizine

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Possible increase in sedation effects	Use concurrently with caution

Adverse Reactions: Meclizine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Sedation, headache, dry mouth, fatigue, and nausea	

Efficacy Monitoring Parameters. Improvement in nausea or vertigo symptoms.

Toxicity Monitoring Parameters. Seek medical attention for signs of severe CNS toxicity.

Key Patient Counseling Points. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery. Patients should avoid alcoholic beverages while taking this drug. Because of its potential anticholinergic action, this drug should be used with caution in patients with asthma, glaucoma, or enlargement of the prostate gland.

Clinical Pearls. Meclizine is available over the counter in many different products, and by prescription. Caution should be used to avoid duplication of therapy and patients should be advised on product selection.

MEDROXYPROGESTERONE: Provera, Various

Class: Progestin Hormone

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg; **Oral Suspension:** 104 mg/0.65 mL, 150 mg/mL, 400 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Abnormal uterine bleeding unrelated to menstrual cycle: 5-10 mg po daily × 5-10 d starting on days 16 or 21 of the menstrual cycle
2. Prevention of estrogen-induced endometrial hyperplasia: 5-10 mg po daily for 12-14 d starting on days 1 or 16 of the menstrual cycle, when estrogen is being administered
3. Secondary physiologic amenorrhea: 5-10 mg po daily × 5-10 d

Off-Label Uses.

1. Breast cancer, endometrial carcinoma: Dose is individualized

Barr generic pictured

MOA. Medroxyprogesterone transforms proliferative into secretory endometrium. Androgenic and anabolic effects have been noted, but the drug is apparently devoid of significant estrogenic activity.

Drug Characteristics: Medroxyprogesterone

Dose Adjustment Hepatic	Mild or moderate hepatic dysfunction, reduce dose or dose frequency; severe, contraindicated	**Absorption**	F = 0.6-10%, food increases AUC and Cmax
Dose Adjustment Renal	Not required	**Distribution**	86-90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate; induces CYP3A4/5
Pregnancy Category	X	**Elimination**	Primarily renal elimination (metabolites) with a half-life of 11-16 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to medroxyprogesterone, abnormal genital bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of DVT or PE, severe liver dysfunction, known or suspected pregnancy	**Black Box Warnings**	Cardiovascular, dementia risk, loss of BMD (Depo-Provera)

Medication Safety Issues: Medroxyprogesterone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	MedroxyPROGESTERone	No	No	Covera, methylPREDNISolone	No

Drug Interactions: Medroxyprogesterone

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased medroxyprogesterone metabolism reduces medroxyprogesterone effectiveness	Consider dose increases of medroxyprogesterone
CYP3A4/5 inhibitors	Decreased medroxyprogesterone metabolism increases risk of medroxyprogesterone toxicity	Consider dose decreases of medroxyprogesterone
CYP3A4/5 substrates	Increased substrate metabolism may decrease effectiveness of substrates	Monitor and consider increasing dose of substrate
Corticosteroids	Clearance of corticosteroid reduced by inhibition of corticosteroid metabolism by the medroxyprogesterone resulting in steroid toxicity	Monitor for corticosteroid toxicity and reduce dose if necessary
Warfarin	Medroxyprogesterone may increase or decrease warfarin effectiveness; mechanism unknown	Monitor INR

Adverse Reactions: Medroxyprogesterone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight gain, headache, amenorrhea, breast tenderness	Abdominal pain, asthenia, feeling nervous, breakthrough bleeding	Deep venous thrombosis, thrombophlebitis, osteoporosis, pulmonary embolism

Efficacy Monitoring Parameters. Resolution of clinical signs of abnormal bleeding.

Toxicity Monitoring Parameters. Baseline pelvic and breast exam at therapy initiation; monitor BMD; diagnostic evaluation to rule out malignancy in the event of persistent or recurring vaginal bleeding.

Key Patient Counseling Points. Menstrual bleeding should occur 3-7 d after last dose. Patients should report if menstruation does not occur within 7 d after last dose.

Clinical Pearls. Injectable formulation of medroxyprogesterone is administered every 3 mo for contraception and for pain associated with endometriosis. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk of myocardial infarction, stroke, invasive breast cancer, PE, and DVT has been shown in postmenopausal women.

MELOXICAM: Mobic, Various

Class: NSAID

Dosage Forms. **Oral Tablet:** 7.5 mg, 15 mg; **Oral Suspension:** 7.5 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Osteoarthritis: 7.5 mg po daily, may titrate to *max* of 15 mg/d
2. Rheumatoid arthritis: 7.5 mg po daily, may titrate to *max* of 15 mg/d
3. Juvenile rheumatoid arthritis: Children ≥2 y of age, 0.125 mg/kg po daily, may titrate to *max* of 7.5 mg/d

Off-Label Uses. None

MOA. Nonselective inhibitor of COX-1 and COX-2, and reversibly alters platelet function and prolongs bleeding time.

Mylan generic pictured

Drug Characteristics: Meloxicam

Dose Adjustment Hepatic	Not required	**Absorption**	F = 89%, food has minimal effect on absorption
Dose Adjustment Renal	Avoid if CrCl <20 mL/min	**Distribution**	Vd = 10-16 L; 99% protein bound
Dialyzable	Not dialyzable, *max* dose 7.5 mg/d	**Metabolism**	Hepatic, minor substrate of CYP3A4/5
Pregnancy Category	C (D ≥30 weeks gestation)	**Elimination**	Renal elimination with a half-life of 15-20 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Sensitivity to meloxicam; concurrent ketorolac, pentoxifylline use, asthma, allergic-type reaction following other NSAID use, CABG	**Black Box Warnings**	Cardiovascular and GI risk, CABG

Medication Safety Issues: Meloxicam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent

Drug Interactions: Meloxicam

Typical Agents	Mechanism	Clinical Management
Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline	Additive GI toxicity and increased risk of bleeding	Concurrent ketorolac, pentoxifylline contraindicated; others, monitor for GI toxicity
ACE-Is, ARBs, beta-blockers, loop and thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
Cholestyramine	Decreased absorption of meloxicam	Separate administration by 1-2 h
Cyclosporine, tacrolimus	Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism	Monitor cyclosporine and tacrolimus levels and consider dose adjustments
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid concurrent use in patients with renal dysfunction
Sulfonylureas	Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism	Monitor FPG and adjust as necessary
Warfarin	Both substrates for CYP2C9, competitive metabolism	Monitor INR and adjust warfarin dose

Adverse Reactions: Meloxicam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity	Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, congestive heart failure, aplastic anemia

Efficacy Monitoring Parameters. Decreased pain and improved range of motion.

Toxicity Monitoring Parameters. CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

Key Patient Counseling Points. Take with food or milk to decrease GI upset. For suspension, shake gently before using.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs.

MEMANTINE: Namenda

Class: *N*-Methyl-d-Aspartate (NMDA) Receptor Antagonist

Dosage Forms. **Oral Solution:** 10 mg/5 mL; **Oral Tablet:** 5 mg, 10 mg; **Oral Capsule, Extended Release:** 7 mg, 14 mg, 21 mg, 28 mg

Common FDA Label Indication, Dosing, and Titration.

1. Alzheimer disease: 5 mg po daily, may titrate dose no more than once per week to target dose of 10 mg po bid

Forest Laboratories 10 mg pictured

Off-Label Uses. None

MOA. Activation of NMDA receptors by glutamate is believed to contribute to the symptomatology of Alzheimer disease. Memantine is believed to act as an uncompetitive (open-channel) NMDA receptor antagonist that binds preferentially to the NMDA receptor–operated cation channels. There is no evidence that memantine prevents or slows neurodegeneration in patients with Alzheimer disease.

Drug Characteristics: Memantine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%, no effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, target dose of 5 mg po bid	**Distribution**	Vd = 9-11 L; 45% protein bound
Dialyzable	Not dialyzable	**Metabolism**	50% and occurs by glucuronidation
Pregnancy Category	B	**Elimination**	Renal elimination is 50% (unchanged) with a half-life of 60-80 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Memantine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	No	Do not chew or crush XR capsule	No	Mesalamine	No

Drug Interactions: Memantine. None known

Adverse Reactions: Memantine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Hypertension, hypotension, syncope, vomiting, dizziness, headache, cough, pain	Stevens-Johnson syndrome, deep venous thrombosis, hepatitis, liver failure, cerebrovascular accident, grand mal seizure, transient ischemic attack, acute renal failure

Efficacy Monitoring Parameters. Improvement in cognitive function and ability to take part in activities of daily living.

Toxicity Monitoring Parameters. Seek medical attention if severe adverse effects occur; BP, eye exams, LFTs, electrolytes, SCr.

Key Patient Counseling Points. May be taken with or without food.

Clinical Pearls. There is sparse evidence that this product is clinically effective in the treatment of Alzheimer disease. It may slow progression but does not reverse or improve symptoms once present.

MENINGOCOCCAL VACCINE: Menactra, Menveo, Menomune, MenHibrix

Class: Vaccine

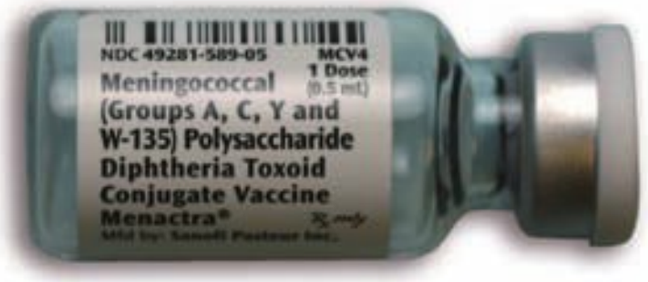
Dosage Forms. **Solution for Intramuscular Injection:** Quadrivalent conjugate vaccine (serogroups A,C,Y,W-135; MCV4) 0.5 mL (Menactra, Menveo); Bivalent conjugate vaccine (serogroups C and Y; MenHibrix); **Solution for Subcutaneous Injection:** Polysaccharide vaccine (MPSV4) 0.5 mL (Menomune)

Common FDA Label Indication, Dosing, and Titration.

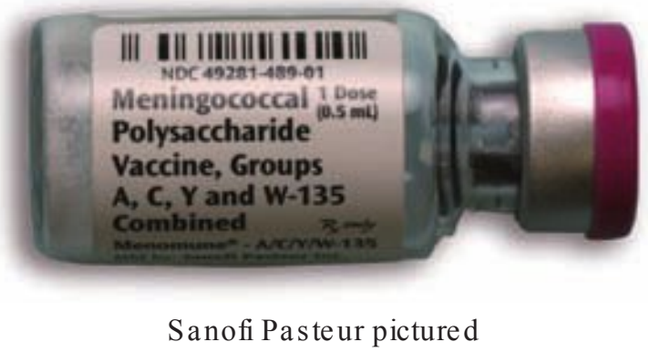
1. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135: Adults, single dose of MCV4 or MPSV4 (through age 55 y for MCV4); Children 2 mo of age, use 4 dose series of Menveo at age 2, 4, 6, and 12 mo; Children 9-23 mo of age, 2 doses of Menactra; Children ≥2 y of age, a single dose of either Menactra or Menveo
2. Prevention of invasive meningococcal disease caused by serotypes C and Y

Off-Label Uses.

1. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135: Routine immunization of adolescents 11-12 y of age and a 2nd dose at 16 y of age
2. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135 in individuals at high risk of invasive meningococcal disease or those at ongoing risk of exposure, in individuals with complement deficiencies, asplenia, HIV, individuals who work with *N. meningitides* in the laboratory: MCV4, 2 doses 3 mo apart and then every 5 y
3. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135 for military recruits, travelers to or people who live in epidemic areas or endemic countries or 1st-year college students up to 21 y of age who live in dormitory and did not receive a dose at 16 y of age: MCV4, single dose



Sanofi Pasteur pictured



Sanofi Pasteur pictured

Drug Characteristics: Meningococcal Vaccine

Pregnancy Category	MCV4, B; MPSV4, B	**ADME**	Not known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to meningococcal vaccine or a component of the vaccine	**Black Box Warnings**	None

Medication Safety Issues: Meningococcal Vaccine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CRM, D	No	No	No	None	No

Drug Interactions: Meningococcal Vaccine

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression may decrease therapeutic effect	Delay meningococcal vaccine administration until corticosteroid therapy has been discontinued if possible; clinical judgment
Immunosuppressing agents: cyclosporine, tacrolimus, azathioprine, methotrexate	Immunosuppression may decrease therapeutic effect	Delay meningococcal vaccine administration until immunosuppressive therapy has been discontinued if possible; clinical judgment

Adverse Reactions: Meningococcal Vaccine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Irritability, abnormal crying, decreased appetite, diarrhea, malaise, fatigue headache, asthenia	Rash, nausea, arthralgia, myalgia, fever	Febrile seizure, anaphylaxis, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of invasive meningococcal disease.

Toxicity Monitoring Parameters. Monitor for syncope after administration.

Key Patient Counseling Points. Used to prevent meningitis and other serious infections. In addition to recommended primary vaccination, patients at risk for infection (asplenic, immune compromised) should receive boosters every 5 y; first-year college students up through age 21 y living in dormitories should be vaccinated if not vaccinated on or after their 16th birthday. Infants at high risk of invasive infection (asplenia, immune compromised) should be immunized starting at age 2 mo with Menveo. Optional MenACWY for healthy infants.

Clinical Pearls. MenACWY-CRM is used to describe Menveo, while MenACWY-D is used to describe Menactra. MenACWY is used to describe all vaccines in this category. Use caution to avoid confusing products. MCV4 should be used to immunize individuals aged 2 mo (Menveo) or 9 mo (Menactra) up to age 55 y. Use MPSV4 for individuals ≥56 y of age who require immunization. MCV4 is administered IM, while MPSV4 is administered SQ. Immunized individuals remain at risk for invasive disease caused by *N. meningitides* serogroup B.

METAXALONE: Skelaxin, Various

Class: Centrally Acting Skeletal Muscle Relaxant

Dosage Forms. Oral Tablet: 800 mg

Common FDA Label Indication, Dosing, and Titration.

1. Musculoskeletal pain or spasm: 800 mg po tid-qid

Off-Label Uses. None

MOA. The mechanism of action of metaxalone in humans has not been established, but may be due to general CNS depression. Metaxalone has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber.

King Pharmaceuticals 800 mg pictured

Drug Characteristics: Metaxalone

Dose Adjustment Hepatic	Use lower initial doses and increase dose carefully	**Absorption**	F is unknown, food enhances absorption
Dose Adjustment Renal	Use lower initial doses and increase dose carefully	**Distribution**	Vd = 800 L
Dialyzable	Not dialyzable	**Metabolism**	Hepatic metabolism, substrate of multiple CYP enzymes
Pregnancy Category	D	**Elimination**	Renal elimination with a half-life of 8-9 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to metaxalone, significantly impaired renal or hepatic function	**Black Box Warnings**	None

Medication Safety Issues: Metaxalone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Mesalamine, metolazone	Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures

Drug Interactions: Metaxalone

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Additive sedative effects	Avoid concurrent use or monitor carefully for signs of toxicity

Adverse Reactions: Metaxalone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea, vomiting, dizziness, headache, somnolence	Hemolytic anemia, leukopenia, jaundice, immune hypersensitivity reaction, maculopapular rash

Efficacy Monitoring Parameters. Reduction in pain and muscle spasms.

Toxicity Monitoring Parameters. Monitor LFTs and CBC periodically.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

Clinical Pearls. Metaxalone is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). Not for use in children <12 y of age. Use with caution in elderly who may be more susceptible to adverse effects.

METFORMIN: Glucophage, Various

Class: Biguanide, Hypoglycemic

Dosage Forms. Oral Tablet: 500 mg, 850 mg, 1000 mg; **Oral Tablet, Extended Release:** 500 mg, 750 mg, 1000 mg; **Oral Solution:** 500 mg/5 mL

Common FDA Label Indication, Dosing and Titration.

1. Diabetes mellitus, type 2: Adults, immediate release, 500-1000 mg po bid, may titrate to *max* dose 2250 mg/d; extended release, 500-2000 mg po daily, may titrate to *max* dose 2000 mg/d; Children ≥10 y of age, immediate release, 500-1000 mg po bid, may titrate to *max* dose 2000 mg/d

Off-Label Uses. None

MOA. Metformin is a biguanide antihyperglycemic agent. It does not affect insulin secretion; rather, it reduces hepatic glucose production and enhances glucose utilization by muscle.

Teva generic 850 mg pictured

Teva generic 1000 mg pictured

Teva generic 500 mg ER pictured

Barr generic 750 mg ER pictured

Drug Characteristics: Metformin

Dose Adjustment Hepatic	Severe hepatic insufficiency, avoid use	**Absorption**	F = 40-60%; immediate release: absorption reduced with food; extended release and oral solution: absorption enhanced with food
Dose Adjustment Renal	SCr >1.4 mg/dL, contraindicated	**Distribution**	Vd = 654 L; not protein bound
Dialyzable	Yes	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	90% renal elimination with a half-life of 7-12 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to metformin, contrast media, SCr >1.4 mg/dL, metabolic acidosis	**Black Box Warnings**	Lactic acidosis

Medication Safety Issues: Metformin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Glucophage and Glucophage XR	MetFORMIN	Do not chew or crush ER formulation	Yes	MetroNIDAZOLE	No

Drug Interactions: Metformin

Typical Agents	Mechanism	Clinical Management
Acetrizoic acid and other contrast media	Increased risk of lactic acidosis and renal failure	Contraindicated
Beta-blockers	Altered glucose metabolism and increased risk of hypoglycemia	Avoid propranol; use others with caution and increased monitoring
Cationic drugs, amiloride, cimetidine, cephalexin	Competition for proximal renal tubular secretion and reduced metformin clearance	Monitor and consider dose adjustments of both agents
Fluoroquinolones	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Metformin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, malabsorption, nausea, cobalamin deficiency, asthenia, vomiting, f atulence	Headaches, indigestion	Lactic acidosis, weight loss, hepatoxicity, hemolytic anemia, hypersensitivity

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity. Renal function, CBC, B_{12} levels. Seek medical attention if severe skin rash, muscle weakness or pain, yellowing of eyes or skin, unusual bruising, or bleeding.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Take with morning meal if daily dosing. Take with morning and evening meal if bid. Drink plenty of liquids to improve elimination of metformin. Avoid alcohol; this increases the risk of lactic acidosis.

Clinical Pearls. Patient having procedure with iodinated contrast: withhold metformin prior to or at the time of the procedure and for 48 h following the procedure. Restart metformin only after kidney function has been reevaluated and found to be normal. Take extended-release product with food or milk. Immediate release may be taken with food, if GI upset occurs. Metformin is first-line therapy for type 2 diabetes. Metformin does not cause hypoglycemia when used as a single agent. Response typically not seen at doses <1500 mg/d.

METHADONE: Dolophine, Various

Class: Opioid Analgesic. C-II

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet for Suspension:** 40 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL, 10 mg/1 mL

Common FDA Label Indication, Dosing, and Titration.

1. Pain, chronic (moderate-severe): Opioid naive patients, 2.5 mg po q8h, may titrate to response
2. Drug detoxification, opioid abuse: 15-30 mg po q8h, titrate to response; when used for treatment of opioid addiction (detoxification or maintenance), may only be dispensed by certified opioid treatment programs

Roxane generic 10 mg pictured

Off-Label Uses. None

MOA. Methadone is a phenylethylamine opioid agonist qualitatively similar to morphine but with a chemical structure unrelated to the alkaloid-type structures of the opium derivatives. Analgesic activity of (R)-methadone is 8-50 times that of (S)-methadone, and (R)-methadone has a tenfold higher affinity for opioid receptors.

Drug Characteristics: Methadone

Dose Adjustment Hepatic	Not required	**Absorption**	F = 85% with minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3.6 L/kg; 85-90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2B6 and 3A4/5 substrate. Moderate CYP2D6 inhibitor
Pregnancy Category	C	**Elimination**	Renal elimination is 10-20% with a half-life of 20-24 h
Lactation	Usually compatible, peak concentration 4-5h after dose	**Pharmacogenetics**	None known
Contraindications	Bronchial asthma, hypersensitivity to opioids, paralytic ileus, respiratory depression, hypercarbia	**Black Box Warnings**	Accidental ingestion; drug abuse; opioid addiction/use; QT prolongation; respiratory depression; tablets contain excipients

Medication Safety Issues: Methadone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Intensol	No	Tablet for suspension	Yes	Dexmethylphenidate, Mephyton	No

Drug Interactions: Methadone

Typical Agents	Mechanism	Clinical Management
Amiodarone, agents that prolong the QT interval	Additive QT prolongation	Avoid concurrent use
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Buprenorphine, opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP3A4/5 and CYP2B6 inducers	Increased methadone metabolism and decreased methadone efficacy	Consider methadone dose increases
CYP3A4/5 and CYP2B6 inhibitors	Decreased methadone metabolism increases risk of methadone toxicity	Consider methadone dose decreases
CYP2D6 substrates	Reduced metabolism of substrates and increased toxicity	Avoid concurrent use or consider dose reduction of substrates
Didanosine	Decreased didanosine absorption	Separate use by 1-2 h
MAOIs	Additive respiratory depression, increased risk of serotonin syndrome	Contraindicated

Adverse Reactions: Methadone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, GI distress, hypotension, dizziness, sedation	Arrhythmias, edema, dyspnea, respiratory depression	Stevens-Johnson syndrome, physical dependence, tolerance, QT prolongation

Efficacy Monitoring Parameters. Relief of pain. Relief of signs and symptoms associated with narcotic addiction.

Toxicity Monitoring Parameters. Seek medical attention if severe skin rash, excessive drowsiness, decreased breathing, severe constipation, chest pain, or dizziness; vital signs.

Key Patient Counseling Points. Use a stool softener and stimulant combination or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Seek medical attention if short of breath or extremely drowsy. Breast-feeding women should monitor child for signs of sedation and respiratory depression.

Clinical Pearls. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. High interpatient variability in absorption, metabolism, and relative analgesic potency of methadone requires careful dose initiation and titration. Fatal respiratory depression has occurred; the highest risk is at initiation and with dosage increases. For oral administration only; excipients to deter use by injection are contained in tablets. Do not chew or swallow tablet for suspension—dissolve in liquid and drink. Keep away from children and pets. Medication guide required at dispensing. Included in REMS program requiring additional education for prescribers.

METHOCARBAMOL: Robaxin, Various

Class: Centrally Acting Skeletal Muscle Relaxant

Dosage Forms. Oral Tablet: 500 mg, 750 mg

Common FDA Label Indication, Dosing, and Titration.

1. Musculoskeletal pain or spasm: 1500 mg po qid × 48-72 h, may titrate to 750 mg po q4h, or 1500 mg po tid or 1000 mg po qid

Qualitest generic pictured

Off-Label Uses. None

MOA. The mechanism of action of methocarbamol in humans has not been established, but may be due to general CNS depression. It has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber.

Drug Characteristics: Methocarbamol

Dose Adjustment Hepatic	Use lower doses initially and increase dose carefully in patients with hepatic failure	**Absorption**	Food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Protein binding 45-50%
Dialyzable	Not dialyzable	**Metabolism**	Hepatic via dealkylation and hydroxylation
Pregnancy Category	C	**Elimination**	Renal elimination of metabolites with a half-life of 1-2 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Methocarbamol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Mephobarbital, Skelaxin	Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures

Drug Interactions: Methocarbamol

Typical Agents	Mechanism	Clinical Management
CNS depressants (opioids, benzodiazepines, alcohol)	Additive sedative effects	Avoid concurrent use or monitor carefully for signs of toxicity

Adverse Reactions: Methocarbamol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Flushing, pruritus, rash, urticaria, nausea, vomiting, dizziness, headache, nystagmus, somnolence, vertigo, blurred vision, conjunctivitis	Bradyarrhythmia, hypotension, syncope, leukopenia, anaphylactoid reaction

Efficacy Monitoring Parameters. Reduction in pain and muscle spasms.

Toxicity Monitoring Parameters. Seek medical attention if idiosyncratic symptoms such as extreme weakness, transient quadriplegia, dizziness, and confusion occur within minutes or hours after 1st dose; vital signs.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

Clinical Pearls. Methocarbamol is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). Drug may color urine brown, black, or green. Injectable form available, used for spasticity associated with tetanus.

METHOTREXATE: Trexall, Various

Class: Antimetabolite

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg

Dava generic 2.5 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Non-Hodgkin lymphoma, advanced (Burkitt lymphoma, stages I and II): 10-25 mg/d po for 4-8 d for several courses with a 7-10 d rest period
2. Psoriasis (Severe): initial, 2.5-5 mg q12h × 3 doses/wk, may titrate dose to 10-25 mg/wk po
3. Rheumatoid arthritis, severe: 7.5-15 mg po once weekly, may titrate by 5 mg/wk every 2-3 wk to *max* 20-30 mg/wk
4. Juvenile rheumatoid arthritis, polyarticular course: 10 mg/m^2 po once weekly, may titrate to clinical response

Off-Label Uses.

1. Many cancers: Dose varies with cancer, stage, and concurrent chemotherapy

MOA. Reversibly inhibits dihydrofolate reductase (DHFR). Dihydrofolates are reduced to tetrahydrofolates by DHFR before they are used in DNA synthesis. Methotrexate interferes with DNA synthesis, repair, and cellular replication.

Drug Characteristics: Methotrexate

Dose Adjustment Hepatic	Bilirubin = 3.1-5 mg/dL, reduce dose by 25%; bilirubin >5 mg/dL, avoid	**Absorption**	Dose-dependent, doses <40 mg/m^2, F = 42%; doses >40 mg/m^2, F = 17%
Dose Adjustment Renal	CrCl = 10-50 mL/min, reduce dose by 50%; CrCl <10 mL/min: avoid	**Distribution**	Vd = 0.4-0.8 L/kg; 50% protein bound
Dialyzable	Yes, hemodialysis	**Metabolism**	Intracellular polyglutamation, excreted by P-glycoprotein
Pregnancy Category	X	**Elimination**	Renal elimination is 48-100% with a dose-dependent half-life of 4-10 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to methotrexate, pregnancy, nursing, preexisting blood dyscrasias in patients treated for psoriasis and rheumatoid arthritis	**Black Box Warnings**	Acute renal failure; ascites; bone marrow suppression; dermatologic toxicity; diarrhea; hepatotoxicity; lymphomas; NSAIDs; opportunistic infections; pneumonitis; renal impairment; tumor lysis syndrome; CBC w/diff, platelet, liver, and renal lab testing mandatory

Medication Safety Issues: Methotrexate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Mercaptopurine, methylPREDNISolone	No

Drug Interactions: Methotrexate

Typical Agents	Mechanism	Clinical Management
Aspirin, dantrolene, loop diuretics, NSAIDs, penicillins, PPIs, salicylates, trimethoprim, sulfisoxazole	Competition for renal tubular secretion, increased methotrexate toxicity and nephrotoxicity	Avoid concurrent use, or consider methotrexate dose reductions. NSAIDs are contraindicated.
BCG vaccine, other live vaccines and immunostimulants	Increased risk of infection from live vaccine	Contraindicated
Eltrombopag	Inhibition of OATP1B1 by eltrombopag results in decreased methotrexate clearance and increased toxicity	Avoid concurrent use, or consider methotrexate dose reductions
Leucovorin, folic acid	Leucovorin is a reduced folate that counteracts the anticancer effects of methotrexate	Avoid concurrent use, unless using as a rescue agent

Adverse Reactions: Methotrexate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Myelosuppression, nausea, vomiting, alopecia, stomatitis, photosensitivity, rash	Elevated LFTs, diarrhea	Acute renal failure, liver failure, interstitial lung disease, Stevens-Johnson syndrome, secondary malignancies (lymphomas), opportunistic infections

Efficacy Monitoring Parameters. Resolution of symptoms of psoriasis. Decreased pain and improved range of motion in rheumatoid arthritis. Shrinkage or disappearance of tumor. Methotrexate levels may be monitored and used to adjust leucovorin.

Toxicity Monitoring Parameters. Baseline and periodic CBC, SCr, LFTs, negative pregnancy test. Seek medical attention if severe mouth ulcerations, fever >101.5°F, shortness of breath, changes in urination, yellowing of eyes or skin, unusual bruising, or bleeding.

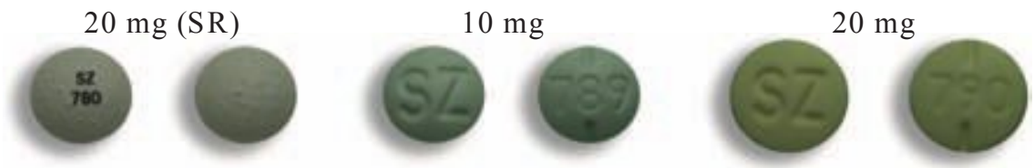
Key Patient Counseling Points. Causes nausea and vomiting; ensure patients have antiemetics and know how to take them. Avoid sun exposure. May take with food.

Clinical Pearls. Baseline and regular CBC w/diff, platelet, liver, and renal lab testing are mandatory. High-dose methotrexate requires urine alkalinization with sodium bicarbonate infusions to enhance methotrexate excretion and requires leucovorin administration started 24 h after methotrexate to rescue normal cells. Elimination is reduced in patients with ascites and/or pleural effusions related to third spacing, resulting in prolonged half-life and toxicity. Concomitant methotrexate administration with radiotherapy may increase the risk of soft tissue necrosis and osteonecrosis. Numerous dosing regimens are used; do not confuse daily and weekly dosing strategies.

METHYLPHENIDATE: Ritalin, Various

Class: CNS Stimulant. C-II

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg, 20 mg; **Oral Tablet, Chewable:** 2.5 mg, 5 mg, 10 mg; **Oral Tablet, Extended Release:** 10 mg, 18 mg, 20 mg, 27 mg, 36 mg, 54 mg; **Oral Capsule, Extended Release:** 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg; **Oral Capsule Extended Release, 24 h:** 10 mg, 20 mg, 30 mg, 40 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL; **Oral Suspension:** 25 mg/5 mL; **Patch:** 10 mg/9 h, 15 mg/9 h, 20 mg/9 h, 30 mg/9 h



Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Attention-deficit hyperactivity disorder: Adults, immediate-release tablets, solution, and chewable tablets, 10-60 mg/d po divided 2-3 times daily, preferably 30-45 min before meals; Children ≥6 y of age, initial, 5 mg po bid, may titrate in increments of 5-10 mg at weekly intervals; doses above 60 mg/d not recommended
2. Attention-deficit hyperactivity disorder, no prior methylphenidate therapy: Adults and Children ≥6 y of age, extended release, 20 mg po daily, may titrate in increments of 10 mg at weekly intervals; *max* 60 mg/d
3. Narcolepsy: Adults, immediate-release tablets, solution, and chewable tablets, 10-60 mg/d po divided 2-3 times daily; sustained release; Adults and Children ≥6 y of age, 20-60 mg/d po divided q8h

Off-Label Uses.

1. Depression: 5-30 mg po daily

MOA. Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. Amphetamines are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

Drug Characteristics: Methylphenidate

Dose Adjustment Hepatic	Not required	**Absorption**	F = 22-25%, minimal food effect
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.6 L/kg; 10-30% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive metabolism, predominately via de-esterification
Pregnancy Category	C	**Elimination**	Renal elimination is 78-98% with a half-life of 3 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to amphetamines, anxiety, agitation, concurrent MAOIs, drug dependence, glaucoma, tics or history of Tourette syndrome, hypertension, angina, heart failure, concurrent isof urane anesthetics	**Black Box Warnings**	Abuse and dependence potential

Medication Safety Issues: Methylphenidate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CD, ER, XL, LA, SR	No	Do not crush or chew ER formulations	No	Methadone	No

Drug Interactions: Methylphenidate

Typical Agents	Mechanism	Clinical Management
Amitriptyline, citalopram, TCAs	Enhanced amphetamine effects from the release of norepinephrine (hypertension, CNS stimulation)	Avoid concurrent use
Citalopram, SSRIs	Increased risk of serotonin syndrome (muscle rigidity, tachycardia, agitation)	Avoid concurrent use if possible, monitor for serotonin syndrome if used together
MAOIs	Hypertensive crisis	Contraindicated within 14 d

Adverse Reactions: Methylphenidate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight loss, loss of appetite, headache, insomnia, irritability	Anxiety, tachycardia, nausea, vomiting	Seizures, spasmodic movement, anemia, thrombocytopenia, psychosis, mania, drug dependence, suicidal thoughts, priapism

Efficacy Monitoring Parameters. Resolution of signs of ADHD, patients should have improved attention span and reduced impulsivity.

Toxicity Monitoring Parameters. BP, HR, and weight. CBC. Seek medical attention if chest pain, seizures, heart palpitations, change in behavior or personality, or hostility. Growth in children.

Key Patient Counseling Points. Avoid late evening doses due to resulting insomnia. Swallow the extended-release capsule whole. Do not crush, break, or chew it. If you cannot swallow the extended-release capsule, you may open it and pour the medicine into a small amount of soft food such as pudding, yogurt, or applesauce. Stir this mixture well and swallow it without chewing. Avoid abrupt discontinuation. For the patch, apply same time each day, alternating hips. Remove after 9 h.

Clinical Pearls. Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and must be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events. Treatment may include drug holidays to assess ongoing need of medication, decrease tolerance, and limit growth suppression. Avoid confusion of multiple different brand names and formulations. Medication guide required at dispensing. Some generic versions of the extended-release product are BX rated and are not interchangeable.

METHYLPREDNISOLONE: Medrol, Various

Class: Adrenal Corticosteroid

Dosage Forms. **Oral Tablet:** 2 mg, 4 mg, 8 mg, 16 mg, 32 mg

Common FDA Label Indication and Dosing.

Dosing for indications listed below: Adults, 4-48 mg po daily; Children, specific dosing parameters not specified; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. Gastrointestinal diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

Sandoz generic 4 mg pictured

Off-Label Uses. None

MOA. Corticosteroids are naturally occurring and synthetic adrenocortical steroids cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

Drug Characteristics: Methylprednisolone

Dose Adjustment Hepatic	Not required	**Absorption**	Well absorbed
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.5 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Primarily renal elimination with a half-life of 2-3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to methylprednisolone or other glucocortosteroids, administration of live vaccines, fungal infections	**Black Box Warnings**	None

Medication Safety Issues: Methylprednisolone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	MethylPREDNISolone	No	No	PrediniSONE	No

Drug Interactions: Methylprednisolone

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased methylprednisolone metabolism increases risk of methylprednisolone toxicity	Monitor for toxicity and reduce methylprednisolone dose if necessary
CYP3A4/5 inducers	Increased methylprednisolone metabolism decreases methylprednisolone efficacy	Monitor for efficacy and consider methylprednisolone dose increases
Fluoroquinolones	Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly	Avoid concurrent use, or monitor carefully for tendon rupture
Phenytoin	Phenytoin increases methylprednisolone metabolism; methylprednisolone can increase or decrease phenytoin metabolism	Monitor methylprednisolone efficacy and phenytoin concentrations
Warfarin	Steroids can either increase or decrease INR in patients taking warfarin	Monitor INR carefully

Adverse Reactions: Methylprednisolone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
GI upset	Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia	Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection

Efficacy Monitoring Parameters. Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

Toxicity Monitoring Parameters. Monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

Key Patient Counseling Points. For short-term treatment, inform patients to take doses with meals to prevent GI upset. For high-dose or longer-term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

Clinical Pearls. Available in a variety of dosage forms for various indications, including ophthalmic preparations. Use lowest effective dose and discontinue as soon as possible to avoid serious long-term adverse effects. Injectable formulations sold by compounding pharmacies have been associated with outbreak of fatal fungal infections.

METOCLOPRAMIDE: Reglan, Various

Class: Dopamine Antagonist

Dosage Forms. Oral Tablet: 5 mg, 10 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/2 mL 10 mg/10 mL; **Oral Dispersible Tablet:** 5 mg

NorthStar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Diabetic gastroparesis: 10 mg po 30 min before meals and at bedtime × 2-8 wk; *max* 12 wk duration
2. Gastroesophageal reflux disease: Adults, 10-15 mg po qid 30 min before meals and at bedtime; Neonates, 0.15 mg/kg po q6h; Infants, 0.1 mg/kg po tid-qid 10-30 min before meals and at hs, *max* dose 0.3-0.75 mg/kg/d × 2 wk to 6 mo

Off-Label Uses.

1. Decreased lactation: 30-45 mg po daily × 7-15 d or 10-15 mg po tid × 7-15 d
2. Nondiabetic gastroparesis: 10 mg po 30 min before meals and at hs for 2-8 wk; *max* 12 wk duration

MOA. Metoclopramide stimulates motility of the upper GI tract without stimulating gastric, biliary, or pancreatic secretions. Its mode of action is unclear. It seems to sensitize tissues to the action of acetylcholine. It is also a dopamine receptor antagonist at dose >5 mg/kg.

Drug Characteristics: Metoclopramide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 80%, minimal food effect
Dose Adjustment Renal	CrCl = 10-50 mL/min, reduce dose by 25%; CrCl <10 mL/min, reduce dose by 50%	**Distribution**	Vd = 3.5 L/kg; 30% protein bound
Dialyzable	2-38% by hemodialysis	**Metabolism**	Hepatic, minor CYP1A2 and CYP2D6 substrate
Pregnancy Category	B	**Elimination**	Renal 75-80%, with a half-life of 5-6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, GI hemorrhage, mechanical obstruction or perforation, pheochromocytoma, concomitant use with drugs likely to cause extrapyramidal reactions, epilepsy	**Black Box Warnings**	Tardive dyskinesia

Medication Safety Issues: Metoclopramide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ODT	No	Dispersible tablet	No	Metolazone, metoprolol, metroNIDAZOLE	Avoid, unless for gastroparesis

Drug Interactions: Metoclopramide

Typical Agents	Mechanism	Clinical Management
Amitriptyline, antipsychotics, bupropion, TCAs	Increased risk of neuroleptic malignant syndrome and extrapyramidal symptoms	Contraindicated
Cabergoline, dopamine agonists	Decreased effect of dopamine agonists	Avoid concurrent use
Cyclosporine, levodopa, tacrolimus	Increased absorption and toxicity	Avoid concurrent use or monitor cyclosporine or tacrolimus levels and adjust dosage; avoid concurrent levodopa
Didanosine	Increased didanosine plasma concentrations	Avoid concurrent use
Digoxin, posaconazole	Decreased GI absorption and decreased efficacy of digoxin, posaconazole	Avoid concurrent use or monitor digoxin levels and adjust dosage
MAOIs	Increased risk of hypertensive crisis	Avoid concurrent use
Linezolid, SSRIs	Increased risk serotonin syndrome	Avoid concurrent use

Adverse Reactions: Metoclopramide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Asthenia, somnolence	Dizziness, headache	Malignant hypertension, arrhythmias, galactorrhea, amenorrhea, gynecomastia, and impotence secondary to hyperprolactinemia, agranulocytosis, dystonia, extrapyramidal reactions, tardive dyskinesia

Efficacy Monitoring Parameters. Reduction in nausea and vomiting.

Toxicity Monitoring Parameters. Seek medical attention if elevated BP, heart palpitation, fluid retention, unusual bruising or bleeding, or involuntary jerking movements.

Key Patient Counseling Points. Take this medicine on an empty stomach, 30 min before each meal and at bedtime. Not for long-term use. If using the oral dispersible tablet, make sure your hands are dry. Place the tablet in your mouth. It should melt quickly. After the tablet has melted, swallow or take a drink of water.

Clinical Pearls. Extrapyramidal reactions may consist of torticollis, facial spasms, urinary retention, and tetanus-like reactions. Young patients receiving high doses are at increased risk. Most patients respond to anticholinergic agents such as benztropine. Tardive dyskinesia is reported with the use of metoclopramide tablets. The symptoms of tardive dyskinesia are characterized by involuntary movements of the tongue, face, mouth, or jaw.

METOPROLOL: Toprol XL, Various

Class: β-Adrenergic Blocker, Cardioselective

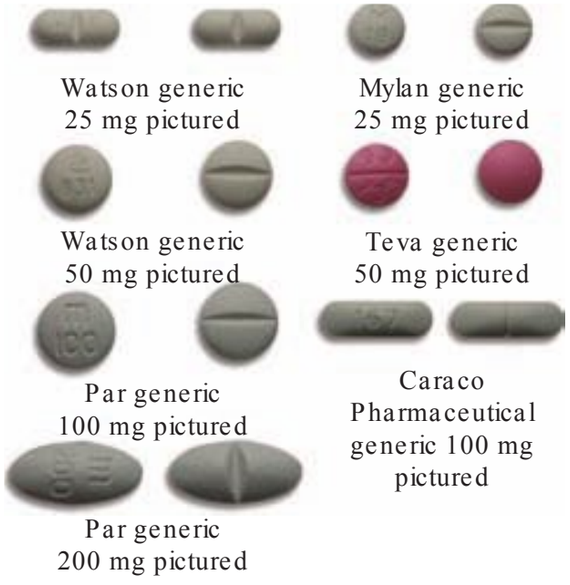
Dosage Forms. Oral Tablet: 25 mg, 50 mg, 100 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 100 mg, 200 mg

Common FDA Label Indication, Dosing, and Titration.

1. Angina: Adults, 50 mg po bid or 100 mg extended release po daily, may titrate to 100-400 mg total daily dose
2. Heart failure: Adults, NYHA Class II, 25 mg po daily for 2 wk, may titrate to *max* 200 mg/d; NYHA Class III-IV, 12.5 mg po daily for 2 wk, may titrate to *max* 200 mg/d
3. Hypertension: Adults, initial, immediate release, 50 mg po bid, may titrate up to 450 mg po per day in 2-3 divided doses; initial, extended release, 25-100 mg po daily, may titrate to 100-400 mg once daily; Children >6 y of age, 1 mg/kg po daily, may titrate to *max* 50 mg/d

Off-Label Uses.

1. Acute myocardial infarction: Adults, immediate release, 25-50 mg po q6-12h, convert to bid dosing over 2-3 d, or to daily extended release dosing with a *max* dose of 200 mg po daily
2. Atrial fibrillation-cardioversion: Adults, 50-200 mg po daily
3. Cardiac dysrhythmia: Adults, immediate release, 25–100 mg po bid; extended release, 50-400 mg po daily



MOA. Metoprolol is a cardioselective β-adrenergic blocker used in arrhythmias, hypertension, angina pectoris, and heart failure. It is also effective in decreasing post-MI mortality.

Drug Characteristics: Metoprolol

Dose Adjustment Hepatic	Liver disease, use slow-dose titration	**Absorption**	F = 65-70%; food increases Cmax and AUC
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3-5 L; 12% protein bound
Dialyzable	Yes, give maintenance dose after dialysis completed	**Metabolism**	Hepatic, CYP2D6 substrate
Pregnancy Category	C	**Elimination**	Renal elimination of metabolite is 95% with a half-life of 3-7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Use with caution in known CYP2D6 poor metabolizers
Contraindications	Hypersensitivity; severe bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome; decompensated heart failure; cardiogenic shock	**Black Box Warnings**	Abrupt withdrawal

Medication Safety Issues: Metoprolol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	No	Do not crush or chew ER formulation ER formulation is scored and can be broken in half	Yes (IV only)	TEGretol, Topamax	No

Drug Interactions: Metoprolol

Typical Agents	Mechanism	Clinical Management
Alpha-blockers, fentanyl	Increased risk of hypotension	Monitor BP
Amiodarone, dronedarone	Increased risk of bradycardia, heart block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
Antidiabetic drugs	Decreased glycemic control	Monitor blood glucose levels
Calcium channel blockers, quinidine	Increased risk of hypotension and/or bradycardia and atrioventricular block	Avoid concurrent use
Clonidine	Exaggerated clonidine withdrawal response	Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy
CYP2D6 inhibitors	Decreased metoprolol metabolism increases risk of metoprolol toxicity	Initiate metoprolol at lower doses, monitor HR and BP
NSAIDs, venlafaxine	Decreased antihypertensive effect of metoprolol	Avoid concurrent use or monitor BP

Adverse Reactions: Metoprolol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, fatigue, hypotension	Arthralgia, bradyarrhythmias, bronchospasm, cold extremities, diarrhea, depression, dyspnea, disorder of glucose regulation, headache, heart block, impotence, nausea, rash, somnolence, syncope, vomiting	Heart failure

Efficacy Monitoring Parameters. Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes, and renal function at baseline and periodically.

Key Patient Counseling Points. Take on an empty stomach and avoid alcohol. Avoid abrupt discontinuation, exacerbations of angina may occur. Instruct patients to report signs/symptoms of hypotension, heart failure, or exacerbation of angina with initial dosing and dose changes. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Advise diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia.

Clinical Pearls. Avoid concomitant use of calcium channel blockers, as concomitant use may significantly affect HR or rhythm. Increase dose weekly when titrating for HTN/angina but every 2 wk for HF. Injectable metoprolol is also used for cardioversion in atrial fibrillation patients.

METRONIDAZOLE: Flagyl, Various

Class: Nitroimidazole Antibiotic, Antiprotozoal

Dosage Forms. Oral Capsule: 375 mg; **Oral Tablet, Extended Release:** 750 mg; **Oral Tablet:** 250 mg, 500 mg

Barr generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Abscess, anaerobic: 7.5 mg/kg po q6h; *max* 4 g/d
2. Amebic dysentery, acute: Adults, 750 mg po tid × 5-10 d; Children, 35-50 mg/kg/d po in 3 divided doses for 10 d; *max* 750 mg/dose
3. Bacterial vaginosis: Extended-release tablets, 750 mg po daily × 7 d
4. Trichomoniasis (for patient and sex partner): 2 g po × 1 dose or 250 mg po q8h × 7 d or 1 g bid × 2 doses

Off-Label Uses.

1. *C. difficile* diarrhea, including pseudomembranous colitis, mild-moderate initial episode or 1st recurrence: 500 mg po tid × 10-14 d
2. *H. pylori* GI tract infection: 500 mg po bid in combination with clarithromycin and a PPI ("triple therapy")

MOA. Metronidazole is a synthetic nitroimidazole active against *T. vaginalis* (trichomoniasis), *E. histolytica* (amebiasis), and *G. lamblia* (giardiasis); it is bactericidal against nearly all obligate anaerobic bacteria including *B. fragilis*.

Drug Characteristics: Metronidazole

Dose Adjustment Hepatic	Severe hepatic dysfunction, consider dose reduction by 50%	**Absorption**	F = 100%, food effects rate, but not extent of absorption
Dose Adjustment Renal	CrCl <10 mL/min, reduce dose by 50%	**Distribution**	Abscess, bronchial f uids, peritoneal, saliva, crosses BBB
Dialyzable	Yes, supplement after hemodialysis, Peritoneal dialysis—no adjustment	**Metabolism**	Hepatic (30-60%) and occurs by glucuronidation. Moderate CYP3A4/5 inhibitor
Pregnancy Category	B	**Elimination**	Renal elimination is 60-80% of unchanged drug with a half-life of ~8 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to metronidazole, 1st trimester of pregnancy	**Black Box Warnings**	Carcinogenic

Medication Safety Issues: Metronidazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ER	MetroNIDAZOLE	Do not crush or chew ER formulation	No	Mebendazole, meropenem, metFORMIN, methotrexate, metoclopramide, miconazole	No

Drug Interactions: Metronidazole

Typical Agents	Mechanism	Clinical Management
Antiarrhythmic agents, TCAs	Increased risk of QT prolongation and other cardiac events	Avoid concurrent use if possible; if used together, monitor carefully and consider dose reductions
Amprenavir oral solution	Contains propylene glycol, an increased risk of propylene glycol toxicity	Solution contraindicated (reaction does not occur with amprenavir capsules)
CYP3A4/5 substrates	Decreases substrate metabolism and increased risk of substrate toxicity	Use with caution and consider dose reductions of CYP3A4/5 substrates. MAOIs are contraindicated
Cholestyramine	Decreased absorption of metronidazole	Separate administration by 2 h
Disulfiram	Increased CNS toxicity and disulfiram reactions	Contraindicated
Warfarin	Increase in warfarin concentration resulting in increase in INR and risk of bleeding	Consider reducing the dose of warfarin; monitor INR and bleeding

Adverse Reactions: Metronidazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headaches, nausea	Diarrhea, dizziness, neuropathy, abnormal taste	Severe hypersensitivity, seizures, ototoxicity, clinically insignificant dark urine, Stevens-Johnson syndrome, neutropenia/thrombocytopenia

Efficacy Monitoring Parameters. Resolution of clinical signs of infection (fever, cultures) within 2-3 d.

Toxicity Monitoring Parameters. Seek medical attention if severe diarrhea, dark urine, yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Monitor CBC for prolonged/repeated courses of therapy.

Key Patient Counseling Points. Avoid alcohol while taking this medicine and for 3 d after, may cause severe disulfiram-like reaction. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Extended-release tablets should be taken on an empty stomach (1 h before or 2 h after meals). Immediate-release tablets and capsules may be administered with food to minimize stomach upset.

Clinical Pearls. May resume normal activities after 24 h of antibiotics and afebrile. Drug of choice for mild-moderate *C. difficile* infection.

MINOCYCLINE: Minocin, Various

Class: Tetracycline Antibiotic

Dosage Forms. **Oral Tablet:** 50 mg, 75 mg, 100 mg; **Oral Tablet, Extended Release:** 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, 135 mg; **Oral Capsule:** 50 mg, 75 mg, 100 mg

Common FDA Label Indication, Dosing, and Titration.

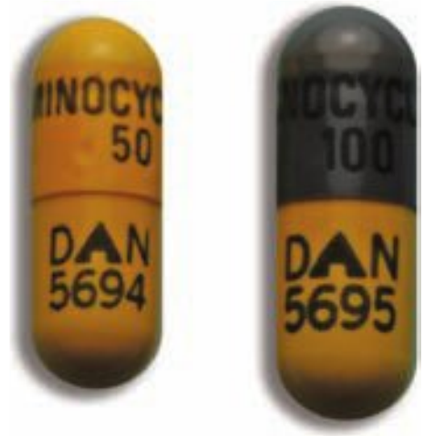
1. Acne vulgaris: Extended-release, 1 mg/kg/d po daily × 12 wk
2. Allergy to penicillin—bacterial infectious disease: Adults, initial, 200 mg po, followed by 100 mg po q12h; Children >8 y of age, 4 mg/kg po, followed by 2 mg/kg/dose q12h (*max* dose 400 mg)

Off-Label Uses.

1. Leprosy: 100 mg po daily

MOA. Tetracyclines are broad-spectrum bacteriostatic compounds that inhibit protein synthesis at the 30S ribosomal subunit. Activity includes gram-positive, gram-negative, aerobic, and anaerobic bacteria, as well as spirochetes, mycoplasmas, rickettsiae, chlamydiae, and some protozoa. Many bacteria have developed plasmid-mediated resistance. Most Enterobacteriaceae and *P. aeruginosa* are resistant.

50 mg 100 mg



Watson generic pictured

Drug Characteristics: Minocycline

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%; can be taken without regard to food
Dose Adjustment Renal	No specific recommendations, but consider dose reduction or extending the interval. Do not exceed 200 mg daily.	**Distribution**	Aqueous humor, CSF, gingival fluids, sinus, saliva, tears
Dialyzable	Not dialyzable	**Metabolism**	Hepatically metabolized, extent unknown
Pregnancy Category	D	**Elimination**	Renal elimination is 10-20% with a half-life of 11-22 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Minocycline

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	ER formulations	No	Indocin, Lincocin, Minizide, niacin, Dyazide, Dynapen	No

Drug Interactions: Minocycline

Typical Agents	Mechanism	Clinical Management
Acitretin	Risk of increased intracranial pressure; mechanism unknown	Concurrent use contraindicated
Aluminum, calcium, and magnesium containing antacids, iron	Decreased absorption via binding	Separate use by 1-2 h
Ethinyl estradiol and other estrogen-based birth control products	Alters intestinal f ora that, in turn, reduces the enterohepatic circulation of estrogen metabolites; decreased efficacy of birth control	Use an alternative form of birth control
Digoxin	Tetracyclines alter bacterial f ora resulting in decreased metabolism of digoxin	Monitor and consider dose adjustments of digoxin
Isotretinoin and vitamin A	Additive risk of intracranial hypertension	Avoid concurrent use
Penicillin	Bacteriostatic drugs, such as the tetracyclines, may interfere with the bactericidal effect of penicillin	Avoid concurrent use

Adverse Reactions: Minocycline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness and vertigo, tooth discoloration in children <8 y of age, headache	Nausea, vomiting, diarrhea, fatigue	Hypersensitivity, hepatotoxicity, renal toxicity, *C. diff cile* colitis, increased intracranial pressure, decreased growth in children

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection, or decreased acne.

Toxicity Monitoring Parameters. Seek medical attention if extreme headache, bloody diarrhea, tooth darkening, or yellowing of the eyes/skin occurs. LFTs, SCr in patients receiving long-term treatment.

Key Patient Counseling Points. May take with food that does not contain calcium (dairy). Complete full course of therapy. Symptoms should improve within 2-3 d if treating infection; if they worsen, seek follow-up with health-care practitioner. Acne should improve within 1-2 wk. Wear sunscreen. Avoid driving or using hazardous machines until side effects are known (dizziness). Warn patients (both male and female) to avoid pregnancy.

Clinical Pearls. Dosing is not interchangeable with extended-release and immediate-release products. Dizziness occurs more frequently in women than men. Less hepatotoxicity than is usually seen with doxycycline. May resume normal activities after 24 h of antibiotics and afebrile. Not for use in children <8 y of age due to bone and tooth discoloration.

MIRTAZAPINE: Remeron, Various

Class: Antidepressant, α_2-Antagonist

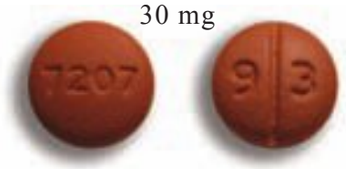
Dosage Forms. Oral Tablet: 7.5 mg, 15 mg, 30 mg, 45 mg; **Oral Disintegrating Tablet:** 15 mg, 30 mg, 45 mg

Common FDA Label Indication, Dosing, and Titration.

1. Depression: 15 mg po daily hs, may titrate to 45 mg po daily hs

15 mg

30 mg



Teva generic pictured

45 mg

Sandoz generic pictured

Off-Label Uses. None

MOA. Mirtazapine is an antidepressant that antagonizes presynaptic α_2-adrenergic auto- and heteroreceptors that are responsible for controlling the release of norepinephrine and serotonin (5-HT). It is also a potent antagonist of postsynaptic 5-HT_2 and 5-HT_3 receptors. The net outcome of these effects is increased noradrenergic activity and enhanced 5-HT activity, especially at 5-HT_{1A} receptors. This unique mechanism of action preserves antidepressant efficacy but minimizes many of the adverse effects common to heterocyclic antidepressants and SSRIs.

Drug Characteristics: Mirtazapine

Dose Adjustment Hepatic	Increase dose slowly as needed and tolerated	**Absorption**	F = 50%; minimal effect of food on absorption
Dose Adjustment Renal	CrCl <40 mL/min, increase dose slowly as needed and tolerated	**Distribution**	Vd = 4.5 L/kg; 85% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5, 2D6 and 1A2 substrate
Pregnancy Category	C	**Elimination**	Renal elimination (metabolites) is 75% and 15% in feces, with a half-life of 20-40 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to mirtazapine; concurrent MAOI, linezolid, IV methylene blue use	**Black Box Warnings**	Suicidality; not for use in children

Medication Safety Issues: Mirtazapine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
SolTab	No	Disintegrating tablet	No	Premarin, ramelteon, Rozerem, Zemuron	No

Drug Interactions: Mirtazapine

Typical Agents	Mechanism	Clinical Management
CYP2D6, CYP3A4/5, and CYP1A2 inducers	Increased metabolism of mirtazapine and decreased efficacy	Avoid concomitant use if possible or consider dose increases of mirtazapine
CYP2D6, CYP3A4/5, and CYP1A2 inhibitors	Decreased metabolism of mirtazapine and increased toxicity	Avoid concomitant use if possible or consider dose decreases of mirtazapine
Fluoxetine, fluvoxamine, linezolid, MAOIs, olanzapine, tramadol, venlafaxine	Increased risk of serotonin syndrome	Avoid concomitant use

Adverse Reactions: Mirtazapine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, increased appetite, somnolence, xerostomia, increased serum cholesterol	Asthenia, dizziness, increased liver enzymes, increased serum triglycerides, weight gain, edema, flu-like symptoms, abnormal thinking	Neutropenia, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; monitor CBC, lipid panel, body weight, and LFTs.

Key Patient Counseling Points. Orally disintegrating tablet blister pack should be opened with dry hands and placed on tongue; no water is needed; tablet should be used immediately after removal from package; once removed, it cannot be stored. Avoid activities requiring mental alertness until drug effects are realized. Report worsening depression, suicidal ideation, or unusual changes in behavior. Do not drink alcohol while taking this drug. Take in the evening prior to sleep.

Clinical Pearls. Safety and effectiveness in pediatric patients have not been established. Use with caution in elderly patients who may be more susceptible to adverse effects. Medication guide required at dispensing. QT prolongation/torsades de pointes has been reported.

MODAFINIL: Provigil, Various

Class: CNS Stimulant. C-IV

Dosage Forms. Oral Tablet: 100 mg, 200 mg

Cephalon pictured

Common FDA Label Indication, Dosing, and Titration.

1. Narcolepsy: 200 mg po daily in the morning, *max* 400 mg/d
2. Obstructive sleep apnea, improve excessive sleepiness; adjunct: 200 mg po daily in the morning, *max* 400 mg/d
3. Shift work-sleep disorder: 200 mg po daily 1 h before start of work shift, *max* 400 mg/d

Off-Label Uses.

1. Attention-deficit hyperactivity disorder: 200 mg po daily

MOA. The mechanism of action of modafinil is uncertain. Modafinil is a wakefulness-promoting agent acting as a CNS stimulant. It is chemically and pharmacologically unrelated to other CNS stimulants, such as methylphenidate, amphetamine, or pemoline.

Drug Characteristics: Modafinil

Dose Adjustment Hepatic	Severe hepatic impairment, 100 mg po daily	**Absorption**	Rapid absorption, food slows absorption but does not affect extent
Dose Adjustment Renal	CrCl <20 mL/min, initial dose 100-200 mg/d	**Distribution**	Vd = 0.9 L/kg; 60% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate. Strong CYP2C19 inhibitor
Pregnancy Category	C	**Elimination**	Renal elimination is 80% (10% unchanged) and 1% in feces, with a half-life of 7.5-15 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Use with caution in CYP2C19 poor metabolizers
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Modafinil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Plaquenil	No

Drug Interactions: Modafinil

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased modafinil metabolism and decreased modafinil efficacy	Avoid concurrent use or monitor efficacy and consider modafinil dose increases
CYP3A4/5 inhibitors	Decreased modafinil metabolism increases risk of modafinil toxicity	Avoid concurrent use or monitor toxicity and consider modafinil dose decreases
CYP2C19 substrates	Decreased metabolism of substrates, increased risk of substrate toxicity	Avoid concurrent use if possible or consider dose reductions of substrates
Combination contraceptives	Decreased contraceptive bioavailability and reduced effectiveness	Use alternative non-hormonal contraceptive method of birth control; monitor closely for signs of breakthrough bleeding and/or pregnancy

Adverse Reactions: Modafinil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Anxiety, headache, insomnia, nausea	Chest pain, dizziness, feeling nervous, hypertension, loss of appetite, palpitations, rash, tachycardia, xerostomia	Cardiac dysrhythmia, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Degree of sleepiness, improvement of mental, and behavioral symptoms.

Toxicity Monitoring Parameters. Palpitations, near syncope, or syncope; may be indicative of a cardiac condition; BP and HR. Weight.

Key Patient Counseling Points. This drug may decrease effectiveness of hormonal or IUD contraception. Recommend additional form of birth control during therapy and 1 mo after last dose. Avoid activities requiring mental alertness or coordination until drug effects are realized. If using drug for daytime wakefulness, take in the morning; if using to maintain wakefulness during shift work, take drug 1 h prior to working. Do not drink alcohol while taking this drug. Practice good sleep hygiene. Does not replace need for CPAP machines in patients with obstructive sleep apnea.

Clinical Pearls. Safety and effectiveness in children <16 y old have not been established. HR and BP should be evaluated at baseline, during routine follow-up within 1-3 mo, and at follow-up visits every 6-12 mo. Increases in BP and HR have been reported with the use of certain ADHD drugs. Dispense with medication safety guide.

MOMETASONE NASAL: Nasonex, Various

Class: Intranasal Corticosteroid

Dosage Forms. Nasal Spray: 50 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Seasonal and perennial allergic rhinitis: Children 2-11 y of age, 1 spray/nostril daily (100 mcg/d); Children ≥12 y of age and Adults, 2 sprays/nostril daily (200 mcg/d)
2. Nasal polyp: 2 sprays/nostril (50 mcg/spray) bid (400 mcg/d), reduce dose to 2 sprays/nostril daily if possible

Off-Label Uses. None

MOA. Mometasone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Schering Corporation pictured

Drug Characteristics: Mometasone Nasal

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal (<2%) absorption after nasal administration
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Mometasone Nasal

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: **Mometasone Nasal.** None known

Adverse Reactions: Mometasone Nasal

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nasal irritation and burning, headache, pharyngitis	Epistaxis, cough	Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis

Efficacy Monitoring Parameters. Control of rhinitis signs and symptoms.

Toxicity Monitoring Parameters. While only small amounts of mometasone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection.

Key Patient Counseling Points. Advise patients on the proper administration technique for this product. Nasal spray needs to be primed before using and if not used for 1 wk. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

Clinical Pearls. Oral inhalation and topical dosage forms of mometasone are also available for treatment of other allergic disorders. While oral antihistamines (either over the counter or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects. May begin treatment for seasonal allergic rhinitis 2-4 wk before the expected start of allergy season at the dose approved for the treatment of allergic rhinitis.

MONTELUKAST: Singulair, Various

Class: Leukotriene Receptor Antagonist

Dosage Forms. **Oral Tablet:** 10 mg; **Oral Chewable Tablet:** 4 mg, 5 mg; **Oral Granules:** 4 mg/packet

Common FDA Label Indication, Dosing, and Titrations.

1. Asthma: Children 12 mo to 5 y of age, 4 mg po daily; Children 6-14 y of age, 5 mg po daily; Children ≥15 y of age and Adults, 10 mg po daily
2. Exercise-induced asthma: Children 6-14 y of age, 5 mg po 2 h before exercise; Children ≥15 y of age and Adults, 10 mg po 2 h before exercise, *max* 1 dose/24 h
3. Seasonal allergic rhinitis: Children 2 to 5 y of age, 4 mg po daily; Children 6-14 y of age, 5 mg po daily; Children ≥15 y of age and Adults, 10 mg po daily

Merck 10 mg pictured

Off-Label Uses.

1. Atopic dermatitis: 10 mg po daily

MOA. Leukotrienes are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils, and bind to leukotriene receptors. Montelukast binds with leukotriene receptors to inhibit physiologic actions of leukotriene.

Drug Characteristics: Montelukast

Dose Adjustment Hepatic	Not required	**Absorption**	F = 63-73%, food decreases bioavailability
Dose Adjustment Renal	Not required	**Distribution**	Vd = 8-11 L; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 and CYP2C9 substrate
Pregnancy Category	B	**Elimination**	Renal elimination is <1% with a half-life of 3-6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Montelukast

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Oralair, SINEquan	No

Drug Interactions: Montelukast

Typical Agents	Mechanism	Clinical Management
CYP2C9 and CYP3A4/5 inducers	Increased metabolism of montelukast decreases montelukast efficacy	Monitor for efficacy of montelukast; consider dose increases
CYP2C9 and CYP3A4/5 inhibitors	Decreased metabolism of montelukast increases the risk of montelukast toxicity	Monitor for toxicity of montelukast; consider dose reductions
Prednisone	Severe peripheral edema	Use with caution; monitor for edema

Adverse Reactions: Montelukast

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Dizziness, fatigue, rash, increased LFTs, dyspepsia	Allergic granulomatosis angiitis, cholestatic hepatitis, aggressive behavior, altered behavior, suicidal thoughts

Efficacy Monitoring Parameters. Resolution of clinical signs of asthma (improved pulmonary function tests) or symptoms of rhinitis.

Toxicity Monitoring Parameters. Seek medical attention if change in behavior/mood, including suicidal thinking or suicide or neuropsychiatric symptoms (eg, agitation, aggression, anxiousness, etc,) occurs; monitor blood chemistry and LFT monitoring.

Key Patient Counseling Points. Not indicated for acute asthma attacks. Report increased use or frequency of short-acting inhaled bronchodilators and advise patients not to discontinue or decrease the dose of other asthma medications unless instructed by a health-care professional. Patients with asthma or allergic rhinitis should take dose in the evening.

Clinical Pearls. Current treatment guidelines published by the National Heart, Lung, and Blood Institute (NHLBI) emphasize the use of inhaled corticosteroids as first-line therapy for long-term control of persistent asthma symptoms in both children and adults. Leukotriene receptor antagonists are alternative agents, but not preferred, for the treatment of mild persistent asthma in children ≥5 y of age, and in adults. Consult guidelines for more information on asthma management.

MORPHINE ER: MS Contin, Avinza, Kadian, Various

Class: Opioid Analgesic. C-II

Dosage Forms. Oral Tablet: 15 mg 30 mg; **Oral Tablet, Extended Release:** 15 mg, 30 mg, 60 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 h:** Avinza: 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg; Kadian: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 80 mg, 100 mg, 200 mg; **Oral Solution:** 10 mg/5 mL, 20 mg/5 mL, 20 mg/1 mL, 100 mg/5 mL; **Rectal Suppository:** 5 mg, 10 mg, 20 mg, 30 mg

15 mg

Endo generic pictured

30 mg

Mallinckrodt generic pictured

60 mg

Endo generic pictured

Common FDA Label Indication and Dosing.

1. Pain, chronic, moderate to severe: 10-20 mg po q12h, titrate to response; use immediate-release formulation to determine patient's morphine requirement and titrate to response. Avinza is given once daily; Kadian may be given once daily or q12h. MS Contin is given q8-12h.

Off-Label Uses. None

MOA. Morphine is a pure mu agonist. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation. It also decreases gastric, biliary, and pancreatic secretion, induces peripheral vasodilation, and promotes opioid-induced hypotension due to histamine release.

Drug Characteristics: Morphine ER

Dose Adjustment Hepatic	Severe impairment, extend dosing interval or start with lower doses	**Absorption**	F = <40%, food slows rate, but not extent of absorption
Dose Adjustment Renal	CrCl 10-50 mL/min, reduce dose by 25%; CrCl <10 mL/min, reduce dose by 50%	**Distribution**	Vd = 1-6 L/kg; 20-36% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic by glucuronidation
Pregnancy Category	C	**Elimination**	Renal elimination (metabolites) is 90% with a half-life of 15 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to opioids, acute or severe asthma, paralytic ileus, respiratory depression, GI obstruction	**Black Box Warnings**	Abuse/misuse/diversion; ethanol; extended release products; concentrated oral solutions; overdose; respiratory depression

Medication Safety Issues: Morphine ER

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	AVINza	ER formulations	Yes	Evista, INVanza, OxyCONTIN, hydromorphone, methadone, magnesium sulfate	No

Drug Interactions: Morphine ER

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Buprenorphine, opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
MAOIs	Additive respiratory depression, increased serotonin syndrome	Contraindicated

Adverse Reactions: Morphine ER

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, nausea, vomiting, hypotension, dizziness, sedation, edema, pruritus, headaches, depression, xerostomia	Dyspnea	Cardiac arrest, physical dependence, tolerance, respiratory depression

Efficacy Monitoring Parameters. Relief of pain.

Toxicity Monitoring Parameters. Excessive drowsiness, decreased breathing, severe constipation, chest pain, dizziness, vital signs.

Key Patient Counseling Points. Use a stool softener and stimulant or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Extended-release products must not be crushed or chewed. Crushing or chewing will release the total dose of morphine at once and increase risk of respiratory depression. ER capsule can be opened and sprinkled on soft food, but must be swallowed whole and not chewed.

Clinical Pearls. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Extended-release products are not for use in children. Fatal respiratory depression has occurred; highest risk at initiation and with dosage increases. Do not administer Avinza with alcoholic beverages or ethanol-containing products, which may disrupt extended-release characteristic of product. Highly concentrated oral solutions are available. Check doses carefully when using highly concentrated oral solutions. The 100 mg/5 mL (20 mg/mL) concentration is indicated for use in opioid-tolerant patients only. Now in an REMS program.

MOXIFLOXACIN: Avelox

Class: Fluoroquinolone Antibiotic

Dosage Forms. **Oral Tablet:** 400 mg

Bayer 400 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute infective exacerbation of chronic obstructive pulmonary disease: 400 mg po daily × 5 d
2. Bacterial sinusitis, acute: 400 mg po daily × 10 d
3. Community-acquired pneumonia: 400 mg po daily × 7-14 d
4. Infection of skin and/or subcutaneous tissue: 400 mg po daily × 7-21 d

Off-Label Uses.

1. Tuberculosis: 400 mg po daily × 6 mo

MOA. Moxifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It has a broad spectrum of activity, including gram-positive and gram-negative organisms, *Chlamydia*, and anaerobes. It is effective for respiratory tract infections caused by *S. pneumoniae*, *H. influenzae*, and others.

Drug Characteristics: Moxifoxacin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%, no food effect, take without regard to meals
Dose Adjustment Renal	Not required	**Distribution**	Abdominal tissue, bronchial mucosa CSF, sinus, sputum
Dialyzable	Not dialyzable	**Metabolism**	52% hepatic via glucuronide and sulfate conjugation
Pregnancy Category	C	**Elimination**	Renal elimination is 20% with a half-life of 12 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	Myasthenia gravis; tendinitis and tendon rupture

Medication Safety Issues: Moxifoxacin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Avonex	No

Drug Interactions: Moxif oxacin

Typical Agents	Mechanism	Clinical Management
Antidiabetic agents	Hypoglycemic or hyperglycemic episodes have been reported when f uoroquinolones were used with antidiabetic agents; mechanism unknown	Caution with concurrent use; monitor plasma glucose and consider dose adjustments of antidiabetic agent
Aluminum, calcium and calcium-fortified foods, didanosine, iron	Decreased absorption of f uoroquinolones caused by chelation	Moxif oxacin should be taken 4 h before or 8 h after agents that decrease moxif oxacin absorption
Class III antiarrhythmic agents or other agents that effect the QTc interval	Additive potential for QTc prolongation	Contraindicated
Corticosteroids	Increased risk of tendon rupture	Counsel patients to discontinue moxif oxacin and seek medical attention if tendon pain or rupture
NSAIDs	Increased risk of seizures via inhibition of GABA resulting in CNS stimulation	Avoid NSAIDs if possible

Adverse Reactions: Moxif oxacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea, dizziness, diarrhea, headache	Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac arrhythmias, liver failure, tendon rupture, psychosis, exacerbation of myasthenia gravis

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection. WBC.

Toxicity Monitoring Parameters. Seek medical attention if decreased urination, yellowing of eyes/skin, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, tendon pain, unusual thoughts, or numbness or tingling in the arms or legs. Baseline renal function tests.

Key Patient Counseling Points. Seek medical attention if rash develops. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If tendon pain develops, discontinue use and seek medical attention. Patients >65 y of age and on concurrent steroids are at increased risk. You may take this medicine with or without food. Do not take this medicine with milk, yogurt, or other dairy products or calcium-fortified products (some juices and breads). If using antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc, take moxifloxacin at least 4 h before or 8 h after these medicines. Wear sunscreen.

Clinical Pearls. Moxifloxacin is not approved for children <18 y of age. Oral and IV dosing is interchangeable. May be used for patients with β-lactam allergy or if initial therapy fails.

MOXIFLOXACIN OPHTHALMIC: Vigamox

Class: Fluoroquinolone Antibiotic, Ophthalmic

Dosage Forms. Ophthalmic Solution: 0.5%

Common FDA Label Indication and Dosing.

1. Bacterial conjunctivitis: Adults and Children >1 y of age, 1 drop to affected eye(s) tid × 7 d

Off-Label Uses. None

MOA. Moxifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It has a broad spectrum of activity, including gram-positive and gram-negative organisms, and anaerobes.

Alcon pictured

Drug Characteristics: Moxifoxacin Ophthalmic

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed after ocular administration
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Moxifoxacin Ophthalmic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Fisamox	No

Drug Interactions: Moxifloxacin Ophthalmic. None known

Adverse Reactions: Moxifoxacin Ophthalmic

Common (>10%)	Less Common (1-10%)	Rare but Serious (>1%)
	Conjunctivitis, dry eyes, eye pain, subconjunctival hemorrhage, tearing and burning of the eyes, reduced visual acuity	Fungal or bacterial ocular superinfection

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection.

Toxicity Monitoring Parameters. Seek medical attention if severe eye pain, itching, redness, or burning.

Key Patient Counseling Points. Symptoms should improve within 2-3 d, but complete full course of therapy. If symptoms worsen, seek follow-up with health-care practitioner. Wash hands with soap and water before and after use. Lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye, but not touching, with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Contact lenses should not be worn during therapy.

Clinical Pearls. Bacterial conjunctivitis is very contagious and spreads by direct contact.

MUPIROCIN: Bactroban, Various

Class: Topical Antibacterial

Dosage Forms. **Topical Ointment:** 2%; **Topical Cream:** 2%; **Nasal Ointment:** 2%

Common FDA Label Indication and Dosing.

1. Impetigo: Apply topically tid × 3-5 d, reevaluate if no response
2. Secondary skin infections: Apply topically tid × 10 d, reevaluate if no response in 3-5 d
3. Eradication of nasal colonization of MRSA during institutional outbreaks: Apply one-half of single use tube to each nostril bid × 5 d

Off-Label Uses.

1. Surgical prophylaxis in MRSA carriers: Apply one-half of single tube to each nostril bid × 5 d

MOA. Mupirocin is an antibacterial agent active against a wide range of gram-positive bacteria including methicillin-resistant *S. aureus*. It is also active against certain gram-negative bacteria. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Because of this unique mode of action, mupirocin demonstrates no in vitro cross-resistance with other classes of antimicrobial agents.

Teva generic 2% ointment pictured

Drug Characteristics: Mupirocin

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption after application to intact skin
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	B	**Elimination**	Not absorbed
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Mupirocin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
AT Nasal	No	No	No	Bacitracin, baclofen, Bactrim	No

Drug Interactions: Mupirocin. None known

Adverse Reactions: Mupirocin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Headache, pruritus, burning at site of application, stinging sensation, rhinitis	*C. diff cile* diarrhea

Efficacy Monitoring Parameters. Resolution of clinical signs of infection within 3-5 d. Eradication of nasal colonization.
Toxicity Monitoring Parameters. Seek medical attention if local adverse effects are severe.
Key Patient Counseling Points. Instruct patients on proper application technique. Avoid drug exposure to open wounds, burns, or eyes.
Clinical Pearls. The area treated may be covered with gauze dressing if desired.

NAPROXEN: Naprosyn, Various

Class: NSAID

Dosage Forms. **Oral Tablet:** 250 mg, 275 mg, 375 mg, 500 mg; **Oral Tablet, Extended Release:** 375 mg, 500 mg, 750 mg; **Oral Tablet, Enteric Coated, Delayed Release:** 375 mg, 500 mg; **Oral Capsule:** 220 mg; **Oral Suspension:** 125 mg/5 mL

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Osteoarthritis: 250-500 mg po bid, extended-release 750-1000 mg po once daily
2. Rheumatoid arthritis: 250-500 mg po bid, extended-release 750-1000 mg po once daily
3. Gout, acute: 250 mg po tid
4. Fever: Adults and Children >12 y of age, 200-400 mg po q8-12h prn, to a *max* of 600 mg daily
5. Pain: Adults, 500 mg po q12h or 25 mg po q6-8h

Off-Label Uses.

1. Migraine: Initial, 750 mg po; may administer an additional 250-500 mg prn, *max* of 1250 mg/24 h

MOA. Nonselective inhibitor of COX-1 and COX-2.

Drug Characteristics: Naproxen

Dose Adjustment Hepatic	Not required, use at lowest effective dose, reduced dose may be considered	**Absorption**	F = 95%, food has minimal effect on absorption
Dose Adjustment Renal	Avoid if CrCl <30 mL/min	**Distribution**	Vd = 0.16 L/kg; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic not via CYP450
Pregnancy Category	C	**Elimination**	Renal elimination is 95% with a half-life of 12-17 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to naproxen, other NSAIDs, aspirin or sulfonamides; asthma or allergic-type reaction following aspirin or other NSAID administration, CABG surgery, treatment of perioperative pain	**Black Box Warnings**	Cardiovascular and GI risk; CABG

Medication Safety Issues: Naproxen

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
DS, DR, EC	No	Do not crush or chew extended-release formulation	No	Natacyn, Anaspaz, Nebcin, Avapro, Naprelan	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent

Drug Interactions: Naproxen

Typical Agents	Mechanism	Clinical Management
Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline	Additive GI toxicity and increased risk of bleeding	Concurrent ketorolac, contraindicated; others, monitor for GI toxicity
Antihypertensive agents: ACE-Is, ARBs, beta-blockers, loop and thiazide diuretics	Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production	Monitor and consider alternative therapy
Cyclosporine, tacrolimus	Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism	Monitor cyclosporine and tacrolimus levels and consider dose adjustments
Pemetrexed	Decreased renal clearance and increased toxicity of pemetrexed	Avoid concurrent use in patients with renal dysfunction
Sulfonylureas	Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism	Monitor FBG and adjust as necessary
Warfarin, rivaroxaban, apixaban, dabigatran	Increased risk of bleeding	Monitor for GI toxicity/bleeding

Adverse Reactions: Naproxen

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity	Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated LFTs, acute renal failure, congestive heart failure, aplastic anemia

Efficacy Monitoring Parameters. Decreased pain and improved range of motion.

Toxicity Monitoring Parameters. Severe skin rash, black tarry stools, chest pain, yellowing of eyes or skin, change in urination; monitor CBC, LFTs, SCr, fecal occult blood tests, BP (if patient has hypertension) if chronic use.

Key Patient Counseling Points. Take with food or milk to decrease GI upset.

Clinical Pearls. Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk of cardiovascular effects. Use lowest dose for shortest period of time to minimize toxicity. Naproxen is also available OTC as a 220-mg tablet. If taken as OTC for fever, do not take longer than 10 d unless directed by physician. Medication guide required at dispensing.

NEBIVOLOL: Bystolic

Class: β-Adrenergic Blocker, Cardioselective, B_1 Selective

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: 5 mg po daily; may titrate to *max* 40 mg po daily

Off-Label Uses.

1. Heart failure: 1.25 mg po daily, may titrate to 10 mg po daily

MOA. Nebivolol is a long-acting cardioselective β_1-adrenoceptor antagonist without intrinsic sympathomimetic activities. The mechanism of action of the antihypertensive response of nebivolol is not fully understood. Possible mechanisms include decreased heart rate, decreased myocardial contractility and vasodilation, and decreased peripheral vascular resistance.

Forest Laboratories 5 mg pictured

Drug Characteristics: Nebivolol

Dose Adjustment Hepatic	Moderate hepatic dysfunction, initial dose 2.5 mg po daily, titrate carefully Severe impairment, avoid	**Absorption**	F = 12% (extensive metabolizers), F = 96% (poor metabolizers); no effect of food on absorption
Dose Adjustment Renal	CrCl <30 mL/min, initial dose 2.5 mg po daily, titrate carefully	**Distribution**	Vd = 695-2755 L; 98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, via CYP2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 38% (extensive metabolizers) to 67% (poor metabolizers) with a half-life of 12-19 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nebivolol; severe bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome; decompensated heart failure, cardiogenic shock; severe hepatic impairment	**Black Box Warnings**	None

Medication Safety Issues: Nebivolol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Nebivolol

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of nebivolol	Avoid concurrent use or monitor BP
Amiodarone, dronedarone	Increased risk of bradycardia, heart block, sinus arrest	Avoid concurrent use in patients with sick sinus syndrome or AV block
Antidiabetic drugs	Decreased glycemic control	Monitor blood glucose levels
Calcium channel blockers	Increased risk of hypotension and/or bradycardia and AV block (non-dihydropyridine)	Monitor BP and HR, may need to avoid with non-dihydropyridines
Digoxin	Increased risk of AV block	Monitor HR, ECG, and serum digoxin concentrations
Alpha-blockers, fentanyl	Increased risk of hypotension	Monitor BP
CYP2D6 inhibitors	Decreased nebivolol metabolism increases risk of nebivolol toxicity	Monitor and consider dose decreases of nebivolol

Adverse Reactions: Nebivolol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Bradyarrhythmias, bronchospasm, disorder of glucose regulation, dizziness, dyspnea, headache, hypotension, nausea, diarrhea, somnolence	Heart block, withdrawal symptoms (angina, myocardial infarction, ventricular arrhythmias)

Efficacy Monitoring Parameters. Decreased BP and HR.

Toxicity Monitoring Parameters. Decreased HR, bronchospasm, blood glucose levels in diabetic patients.

Key Patient Counseling Points. Report signs/symptoms of hypotension, worsening heart failure, or bronchospastic disease. Do not drink alcohol. May cause dizziness. Avoid activities that could be dangerous if not alert. Diabetic patients should carefully monitor blood sugar levels as beta-blockers may mask symptoms of hypoglycemia. Do not discontinue drug abruptly, as this may cause rebound angina or, in some cases, myocardial infarction.

Clinical Pearls. Safety and efficacy not established in children. Patients should avoid concomitant use of calcium channel blockers, as concomitant use may significantly affect HR or heart rhythm.

NIACIN: Niaspan, Slo-Niacin, Various

Abbott Laboratories pictured

Class: Antihyperlipidemic

Dosage Forms. **Oral Capsule, Extended Release:** 250 mg, 500 mg; **Oral Tablet:** 50 mg, 100 mg, 250 mg, 500 mg; **Oral Tablet, Extended Release:** 250 mg, 500 mg, 750 mg, 1000 mg

Common FDA Label Indication, Dosing, and Titration.

1. Coronary arteriosclerosis, hypercholesterolemia: Extended release, 500 mg po daily, may titrate to 2000 mg/d po
2. Dyslipidemia: Adults, immediate release, 100-1000 mg po tid, may titrate to 3000 mg/d po; extended release, 500-2000 mg po daily hs, may titrate to 2000 mg/d po; Children, 100-250 mg/d in 3 divided doses with meals, may titrate to 10 mg/kg/d
3. Myocardial infarction, secondary prophylaxis: Extended release, 500-2000 mg po daily hs, may titrate to 2000 mg/d po

Off-Label Uses.

1. Pellagra: 50-100 mg po tid-qid, may titrate to 500 mg/d po

MOA. Not well defined. May involve partial inhibition of release of free fatty acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL.

Drug Characteristics: Niacin

Dose Adjustment Hepatic	Contraindicated in patients with significant or unexplained hepatic dysfunction	**Absorption**	F = 60%, fatty meals decrease absorption
Dose Adjustment Renal	Not required, use caution	**Distribution**	Unknown
Dialyzable	Unknown	**Metabolism**	Hepatic not via CYP450
Pregnancy Category	C	**Elimination**	Renal elimination is 60-88% with a half-life of 20-45 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to niacin, active liver disease, PUD, arterial hemorrhage	**Black Box Warnings**	None

Medication Safety Issues: Niacin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Slo	No	Long-acting formulations	No	Minocin	No

Drug Interactions: Niacin

Typical Agents	Mechanism	Clinical Management
Statins, colchicine	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use, or monitor for myopathy and consider dose reductions
Cholestyramine, colestipol	Decreased absorption of niacin	Separate administration by 1 h before or 4 h after

Adverse Reactions: Niacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Flushing	Atrial fibrillation, pruritus, rash, nausea, vomiting, reduced platelet count, elevated LFTs, myalgia	Hypophosphatemia, hepatotoxicity, rhabdomyolysis

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL, and triglycerides levels; increase in HDL.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain, monitor LFT, CBC; serum creatine kinase if muscle pain occurs, FBG or HbA_{1c}, uric acid

Key Patient Counseling Points. Start with a low dose and titrate based on tolerability (primarily flushing). Avoid alcohol and warm beverages with niacin to reduce flushing. If discontinued for several days, may need to restart on a lower dose and retitrate. Aspirin or NSAID 30 min prior to niacin may reduce flushing. Take at bedtime with a low-fat snack to help with flushing.

Clinical Pearls. Also known as vitamin B_3. Statins are first-line therapy for hyperlipidemia. Niacin may be added for high-risk patients not able to achieve lipid goals with statin therapy.

NIFEDIPINE: Adalat CC, Procardia XL, Various

Class: Calcium Channel Blocker

Dosage Forms. **Oral Tablet, Extended Release:** 30 mg, 60 mg, 90 mg; **Oral Capsule:** 10 mg, 20 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, 30 mg po daily, may titrate to 90 mg/d po (Adalat CC) or 120 mg/d po (Procardia XL); Children, 0.25 mg/kg po daily in 1 or 2 divided doses, may titrate to 3 mg/kg/d po (*max* of 180 mg/d)
2. Stable chronic angina: 30-60 mg po daily, may titrate to 120 mg/d po
3. Variant angina: 30-60 mg po daily, may titrate to 120 mg/d po

Off-Label Uses.

1. Raynaud phenomenon: 30-60 mg po daily

MOA. Nifedipine is a calcium ion influx inhibitor that selectively inhibits the transmembrane influx of calcium ions into cardiac muscle and smooth muscle. Nifedipine does not alter serum calcium concentrations.

Drug Characteristics: Nifedipine

Dose Adjustment Hepatic	Clearance is reduced in patients with cirrhosis, use with caution	**Absorption**	Complete absorption, food delays absorption of Adalat CC
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.4-202 L/kg; 92-98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 70-80% with a half-life of ~7 h (Adalat CC)
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nifedipine, cardiogenic shock, concurrent CYP3A4/5 inducers	**Black Box Warnings**	None

Medication Safety Issues: Nifedipine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CC, XL	NIFEdipine	Extended-release tablets	No	niCARdipine, niMODipine, nisoldipine, Cartia XT	Avoid immediate release. Potential for hypotension; risk of precipitating myocardial ischemia

Drug Interactions: Nifedipine

Typical Agents	Mechanism	Clinical Management
NSAIDs	Decreased antihypertensive effect of nifedipine	Avoid concurrent use or monitor BP
Amiodarone	Increased amiodarone concentrations and toxicity which may result in bradycardia, AV block, or sinus arrest	Caution is advised, may avoid concurrent use
Beta-blockers	Increased hypotension, bradycardia	Avoid concurrent use or monitor BP and HR
Clopidogrel	Decreased antiplatelet activity of clopidogrel	Avoid concurrent use
CYP3A4/5 inducers	Increased nifedipine metabolism reduces nifedipine effectiveness	Avoid concurrent use or consider dose increases of nifedipine
CYP3A4/5 inhibitors	Decreased nifedipine metabolism increases risk of nifedipine toxicity	Avoid concurrent use or consider dose decreases of nifedipine
Tacrolimus	Increased risk of tacrolimus toxicity	Monitor plasma concentrations
Quinidine	Decreased efficacy of quinidine, increased risk of nifedipine toxicity	Monitor quinidine plasma concentrations, monitor BP

Adverse Reactions: Nifedipine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Flushing, headache, peripheral edema, dizziness	Constipation, fatigue, gastroesophageal ref ux, hypotension, myalgia, myocardial infarction, nausea, palpitations, pruritus, rash, sleep disturbances, gingival hyperplasia,	Aplastic anemia, thrombocytopenia, angina, tachycardia

Efficacy Monitoring Parameters. BP, reduction in chest pain, decreased number of angina attacks, reduction in use of nitroglycerin to relieve chest pain.

Toxicity Monitoring Parameters. Signs/symptoms of peripheral edema, angina, tachycardia, heart failure.

Key Patient Counseling Points. Take Adalat CC on an empty stomach. Report signs/symptoms of hypotension, exacerbation of angina, peripheral edema, fatigue, or hypotension. Do not drink alcohol. Avoid sudden discontinuation of drug as this may cause rebound hypertension. May cause dizziness; avoid driving or using hazardous machinery until effects are known. Avoid grapefruit juice.

Clinical Pearls. With Adalat CC, two 30-mg tablets may be interchanged for one 60-mg tablet, but using three 30-mg tablets results in 29% higher peak plasma concentrations than a single 90-mg tablet; not considered interchangeable.

NITAZOXANIDE: Alinia

Class: Antiprotozoal

Dosage Forms. Oral Tablet: 500 mg; **Oral Suspension:** 100 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Diarrhea caused by *C. parvum* or *G. lamblia*: Adults and Children ≥12 y of age, 500 mg po q12h × 3 d; Children 1-3 y of age, 100 mg po q12h × 3 d; Children 4-11 y of age, 200 mg po q12h × 3 d

Off-Label Uses.

1. *C. difficile*–associated diarrhea: 500 mg po q12h × 10 d

MOA. Interference with the pyruvate ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction, which is essential to anaerobic metabolism of protozoans.

Romark 500 mg pictured

Drug Characteristics: Nitazoxanide

Dose Adjustment Hepatic	Use with caution	**Absorption**	F <5%, food enhances absorption by 50%
Dose Adjustment Renal	Use with caution	**Distribution**	98-99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Metabolized to 1 active metabolite by plasma esterases
Pregnancy Category	B	**Elimination**	33% renal, 67% fecal
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nitazoxanide	**Black Box Warnings**	None

Medication Safety Issues: Nitazoxanide

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Nitazoxanide. None known

Adverse Reactions: Nitazoxanide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea, vomiting, diarrhea, headache, abdominal pain	Elevated LFTs

Efficacy Monitoring Parameters. Resolution of signs and symptoms of infection, improvement in diarrhea.

Toxicity Monitoring Parameters. Consider LFTs and CBC prior to therapy.

Key Patient Counseling Points. Complete full course of therapy; take with food. Store suspension at room temperature (expiration = 1 wk).

Clinical Pearls. Suspension bioavailability is 70% of tablet, not interchangeable. Preferred agent for treating *Cryptosporidium* diarrhea in immunocompetent adults; has not been proven to be superior to placebo in HIV-infected individuals. Equivalent efficacy to metronidazole for *C. difficile* and *Giardia*, however, based on cost metronidazole remains the treatment of choice.

NITROFURANTOIN: Macrodantin, Macrobid, Various

Class: Nitrofuran Antibiotic

Dosage Forms. Oral Capsule: 25 mg, 50 mg, 100 mg;

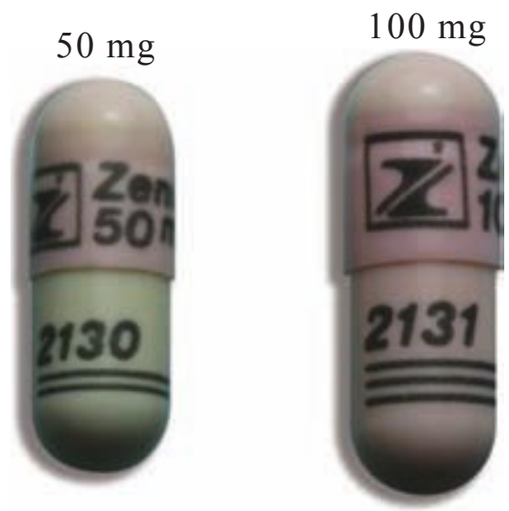
Oral Suspension: 25 mg/ 5mL; **Oral Capsule, Extended Release:** 100 mg

Common FDA Label Indication, Dosing, and Titration.

1. Urinary tract infection treatment: Adults and Children >12 y of age, Macrobid 100 mg po bid × 7 d; Furadantin, Macrodantin, 50-100 mg po q6h × 7 d; Children ≥1 mo of age, 5-7 mg/kg/d in divided doses q6h po × 7 d (*max* 400 mg/d)
2. Urinary tract infection prophylaxis: Adults, Furadantin, Macrodantin, 50-100 mg po daily hs; Children ≥1 mo of age, 1 mg/kg/d po in divided doses every 12-24 h (*max* dose 100 mg/d)

Off-Label Uses. None

MOA. Nitrofurantoin is a synthetic nitrofuran that inactivates bacterial ribosomes and is bactericidal in urine at therapeutic doses. It is active against most bacteria that cause UTIs except nearly all strains of *Pseudomonas* are resistant.



Teva generic pictured

Drug Characteristics: Nitrofurantoin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 94%, food increases absorption
Dose Adjustment Renal	Contraindicated if CrCl <60 mL/min	**Distribution**	90% protein bound
Dialyzable	Yes, hemodialysis only	**Metabolism**	Metabolism in all tissues to inactive metabolite
Pregnancy Category	B, contraindicated in pregnancy at term	**Elimination**	Renal elimination is 40% with a half-life of 1 h
Lactation	Usually compatible	**Pharmacogenetics**	Those with G6PD deficiency are more likely to develop hemolytic anemia
Contraindications	Hypersensitivity to nitrofurantoin, use in neonates or during delivery (risk of hemolytic anemia), anuria or oliguria	**Black Box Warnings**	None

Medication Safety Issues: Nitrofurantoin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not open capsules	No	Nitro-Bid, nitroglycerine, microK, Neurontin, nitroglycerin	Avoid for long-term suppression; avoid in patients with CrCl <60 mL/min

Drug Interactions: Nitrofurantoin

Typical Agents	Mechanism	Clinical Management
Fluconazole	Increased risk of hepatic and pulmonary toxicity, unknown mechanism	Avoid concurrent use, or increase monitoring of toxicity
Norfloxacin	Antagonism of the antibacterial effect of norfloxacin	Avoid concurrent use

Adverse Reactions: Nitrofurantoin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, headache, discoloration of urine	Diarrhea	Severe hypersensitivity, hepatic failure, hemolytic anemia, interstitial lung disease

Efficacy Monitoring Parameters. Resolution of clinical signs of infection within 2-3 d.

Toxicity Monitoring Parameters. Severe diarrhea, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

Key Patient Counseling Points. May make urine brown; this is not harmful and is a breakdown product of the drug. Complete full course of therapy. For the suspension, shake well and store at room temperature, use within 30 d. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up care.

Clinical Pearls. Nitrofurantoin does not reach effective levels in tissue and is only indicated for UTIs (not pyelonephritis). May resume normal activities after 24 h of antibiotics if afebrile. The drug is used primarily to prevent recurrent UTIs but is also effective in the treatment of uncomplicated UTIs.

NITROGLYCERIN: Minitran, Nitro-Dur, Nitrostat, Various

Class: Nitrate, Antianginal

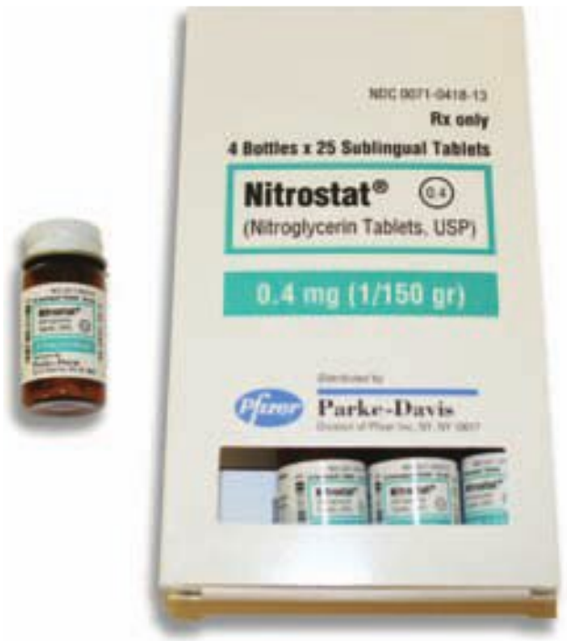
Dosage Forms. **Oral Capsule, Extended Release:** 2.5 mg, 6.5 mg, 9 mg; **Sublingual Tablet:** 0.3 mg, 0.4 mg, 0.6 mg; **Patch:** 0.1 mg/h, 0.2 mg/h, 0.3 mg/h, 0.4 mg/h, 0.6 mg/h, 0.8 mg/h; **Sublingual Spray:** 0.4 mg/actuation; **Ointment:** 2%

Common FDA Label Indication, Dosing, and Titration.

1. Angina, prophylaxis: Extended release, 2.5-6.5 mg po tid-qid; Sublingual, 1 tab or 1-2 sprays 5-10 min before activity, which may induce angina; Transdermal, 0.2-0.4 mg/h worn topically 12-14 h per day, may titrate to 0.8 mg/h worn topically
2. Angina, acute: Sublingual, 1 tab or 1-2 sprays at first sign of angina, repeat every 5 min if needed for total of 3 tabs or doses in 15 min

Off-Label Uses. None

MOA. Nitroglycerin is believed to be converted to nitric oxide (NO) by vascular endothelium. NO activates guanylate cyclase, increasing cyclic GMP that in turn decreases intracellular calcium, resulting in direct relaxation of vascular smooth muscle. In myocardial ischemia, nitrates dilate large epicardial vessels, enhance collateral size and flow, and reduce coronary vasoconstriction.



Pfizer 0.4 mg pictured

Drug Characteristics: Nitroglycerin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 38-75%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3 L/kg; 60% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic not via CYP
Pregnancy Category	C	**Elimination**	Renal elimination is 22% with a half-life of 2-3 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nitrates, concurrent use with erectile dysfunction meds, symptomatic hypotension, severe anemia or increased intracranial pressure	**Black Box Warnings**	None

Medication Safety Issues: Nitroglycerin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
BID, DUR, TIME	No	Extended-release capsules	No	Macrobid, NicoDerm, nitrofurantoin, nitroprusside, Nizoral, Nilstat, nystatin	No

Drug Interactions: Nitroglycerin

Typical Agents	Mechanism	Clinical Management
Phosphodiesterase inhibitors	Excessive hypotension	Concurrent use contraindicated

Adverse Reactions: Nitroglycerin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Headache	Bradycardia, drug tolerance, flushing, hypotension, light-headedness, nausea, orthostatic hypotension, tachycardia, vomiting	Increased intracranial pressure, severe hypotension, syncope, methemoglobinemia

Efficacy Monitoring Parameters. Decreased use of sublingual nitroglycerin to treat anginal episodes, reduction in angina episodes, reduction in anginal pain.

Toxicity Monitoring Parameters. Signs/symptoms of hypotension, problematic headaches, or decreasing efficacy (drug tolerance). BP and HR.

Key Patient Counseling Points. Sit prior to using sublingual tablets, lingual aerosol, or spray. Tablet should be dissolved under tongue or in buccal pouch at 1st sign of angina; do not swallow. Spray should be sprayed onto or under tongue; do not inhale; do not spit out or rinse mouth after use. Rise slowly from a sitting position in order to prevent light-headedness. Allow a 10- to 12-h/d drug-free interval to avoid development of nitrate tolerance for both patches and extended-release capsules. Avoid concurrent use of alcohol, CNS depressants, antihypertensives, or other drugs that cause hypotension. Do not use with phosphodiesterase inhibitors, which may result in hypotension. The ointment may stain clothing.

Clinical Pearls. Safety and efficacy not established in children. Patch contains aluminum; remove before MRI.

NORTRIPTYLINE: Pamelor, Various

Class: Tricyclic Antidepressant

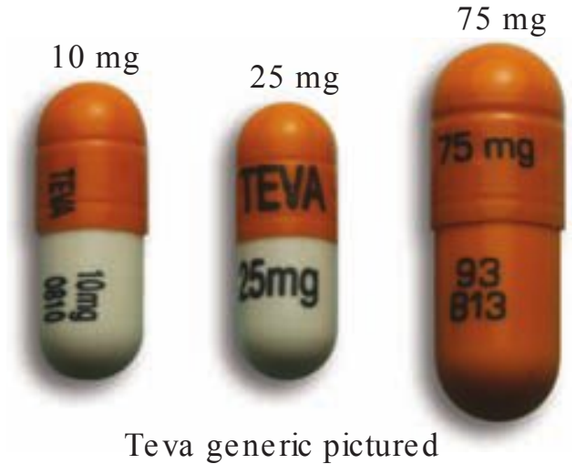
Dosage Forms. Oral Tablet: 10 mg, 25 mg, 50 mg, 75 mg; **Oral Solution:** 10 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Adults, 25 mg po tid-qid, may titrate to 150 mg/d po; Adolescents, 30-50 mg/d po in single or divided doses

Off-Label Uses. None

MOA. Nortriptyline is the demethylated metabolite of amitriptyline, a heterocyclic antidepressant that blocks presynaptic reuptake of norepinephrine with subsequent downregulation of adrenergic receptors. Heterocyclic antidepressants have less effect on serotonergic activity than on other neurotransmitters.



Teva generic pictured

Drug Characteristics: Nortriptyline

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 15-27 L/kg; 86-95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2D6 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 2% with a half-life of 15-39 h
Lactation	Compatible	**Pharmacogenetics**	Caution with CYP2D6 poor metabolizers; at risk for drug interactions and greater toxicity
Contraindications	Hypersensitivity to nortriptyline or other TCAs; concurrent MAOI; use during acute recovery period after MI, patient using linezolid or IV methylene blue	**Black Box Warnings**	Suicidality

Medication Safety Issues: Nortriptyline

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Amitriptyline, Demerol, Bentyl, desipramine, Norpramin, Tambocor	No

Drug Interactions: Nortriptyline

Typical Agents	Mechanism	Clinical Management
Amphetamines	Increased risk of hypertension, cardiac effects, and CNS stimulation	Use caution with concomitant therapy
Linezolid, MAOIs, methylene blue, SSRIs	Increased risk of serotonin syndrome	Concomitant use with MAOIs contraindicated, others with caution
Antiarrhythmics, and drugs that cause QT prolongation	Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest)	Avoid concurrent use
CYP2D6 inhibitors	Decreased metabolism of nortriptyline increases risk of nortriptyline toxicity	Avoid concurrent use

Adverse Reactions: Nortriptyline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation	Blurred vision, confusion, constipation, dizziness, headache, sexual dysfunction, somnolence, urinary retention, weight gain, xerostomia	Cardiac dysrhythmia, heart block, hepatotoxicity, seizures, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior; monitor ECG and LFTs, BP, weight. Signs and symptoms of serotonin syndrome.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause somnolence and dizziness. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol while taking this drug.

Clinical Pearls. Symptomatic improvement may not be seen for several weeks. Medication guide required at dispensing.

NYSTATIN SYSTEMIC: Bio-Statin, Various

Class: Polyene Antifungal

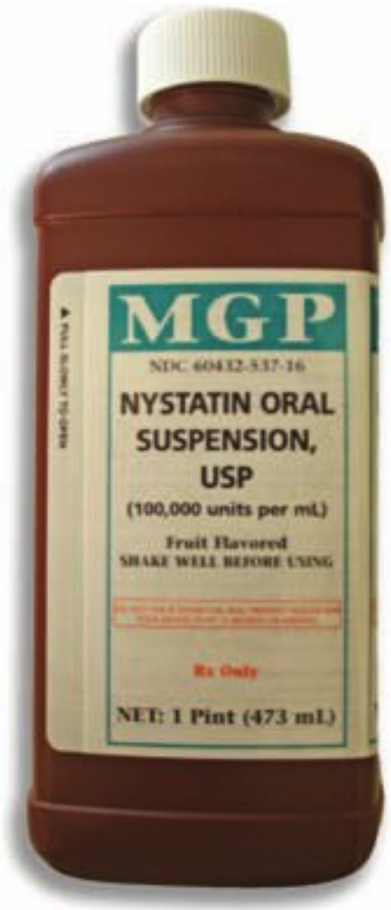
Dosage Forms. Oral Suspension: 100,000 units/mL; **Oral Tablet:** 500,000 units; **Oral Capsule:** 500,000 units, 1,000,000 units

Common FDA Label Indication, Dosing, and Titration.

1. GI candidiasis, nonesophageal: 500,000-1,000,000 units po tid
2. Oropharyngeal candidiasis: 400,000-600,000 units po qid (retained in mouth as long as possible prior to swallowing)

Off-Label Uses. None

MOA. Nystatin binds to the sterols in fungal cell walls, damaging the fungal cell wall membrane and altering its permeability.



MGP generic pictured

Drug Characteristics: Nystatin Systemic

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption
Dose Adjustment Renal	Not required	**Distribution**	Minimal absorption
Dialyzable	Unknown	**Metabolism**	Minimal absorption
Pregnancy Category	C	**Elimination**	Unknown
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nystatin	**Black Box Warnings**	None

Medication Safety Issues: Nystatin Systemic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	HMG-CoA agents (“statins”)	No

Drug Interactions: Nystatin Systemic. None known

Adverse Reactions: Nystatin Systemic

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	GI distress, nausea, vomiting constipation	Rash

Efficacy Monitoring Parameters. Resolution of clinical symptoms.
Toxicity Monitoring Parameters. Seek medical attention if severe mucosal irritation or rash occurs.
Key Patient Counseling Points. Store the oral liquid or tablets at room temperature. Shake suspension well before using.
Clinical Pearls. As effective as clotrimazole in treating topical *Candida* infections. Nystatin is not absorbed and will not treat systemic infections.

NYSTATIN TOPICAL: Mycostatin, Nyamyc, Nystop, Various

Fougera generic ointment pictured

Class: Polyene Antifungal

Dosage Forms. **Topical Cream:** 100,000 units/g; **Topical Ointment:** 100,000 units/g; **Topical Powder:** 100,000 units/g

Common FDA Label Indication, Dosing, and Titration.

1. Candidiasis of skin (cutaneous and mucocutaneous infections): Apply liberally to affected areas topically bid until healing complete

Off-Label Uses. None

MOA. Nystatin binds to the sterols in fungal cell walls, damaging the fungal cell wall membrane and altering its permeability.

Drug Characteristics: Nystatin Topical

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Unknown	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Unknown
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to nystatin	**Black Box Warnings**	None

Medication Safety Issues: Nystatin Topical

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
AF	No	No	No	HMG-CoA agents ("statins"), Nitrostat	No

Drug Interactions: **Nystatin Topical**. None known

Adverse Reactions: Nystatin Topical

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dry skin, skin irritation	Rash, hypersensitivity reaction, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Resolution of clinical symptoms.

Toxicity Monitoring Parameters. Severe skin irritation or rash.

Key Patient Counseling Points. Apply to affected area of skin. Skin should be intact. Do not get it in eyes, nose, or mouth. Avoid occlusive dressings, tight-fitting diapers, and plastic pants if using on diaper area of children.

Clinical Pearls. As effective as clotrimazole in treating topical *Candida* infections. Vaginal tablet for vaginal *Candida* infections is still available but infrequently used. Miconazole and terconazole are both more effective than nystatin and are available OTC for vaginal candidiasis.

OLANZAPINE: Zyprexa, Various

Class: Thienobenzodiazepine, Antipsychotic

Dosage Forms. **Oral Tablet:** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg; **Oral Disintegrating Tablet:** 5 mg, 10 mg, 15 mg, 20 mg

Lilly pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disorder, acute mixed or manic episodes: Adults, 10-15 mg/d po, may titrate in 5 mg/d increments; Children 13-17 y of age, 2.5-5 mg/d po, may titrate in 2.5-5 mg/d increments
2. Schizophrenia: Adults, 5-10 mg/d po, may titrate in 5 mg/d increments at 1-wk intervals to 10-20 mg/d po; Children 13-17 y of age, 2.5-5 mg/d po, may titrate in 2.5-5 mg increments
3. Depression, treatment resistant, in combination with fluoxetine: Adults, 2.5-20 mg po daily

Off-Label Uses. None

MOA. Olanzapine is an atypical antipsychotic agent that is a potent serotonin-5-HT_2 and dopamine-D_2 antagonist. Antipsychotic effect is most likely related to blockade of postsynaptic dopaminergic receptors in the mesolimbic and prefrontal cortexes of the brain, although other neurotransmitter systems also are involved.

Drug Characteristics: Olanzapine

Dose Adjustment Hepatic	Not required, except when used with fluoxetine (limit initial olanzapine dose to 2.5-5 mg daily)	**Absorption**	Well absorbed, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1000 L; 93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic via glucuronidation, CYP1A2 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 57% with a half-life of 21-54 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to olanzapine	**Black Box Warnings**	Mortality in elderly patients with dementia-related psychosis; coma and excessive sedation with injectable formulation

Medication Safety Issues: Olanzapine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	ZyPREXA, OLANZapine	Disintegrating tablet	No	CeleXA, ZyrTEC, olsalazine, QUEtiapine, Reprexain, Zestril, Zelapar, zolpidem	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others

Drug Interactions: Olanzapine

Typical Agents	Mechanism	Clinical Management
Tramadol	Additive serotonergic effects	Avoid concurrent use or monitor for adverse effects
Haloperidol	Increased risk of parkinsonism	Monitor for signs of parkinsonism; adjust haloperidol dose
Metoclopramide	Increased risk of extrapyramidal symptoms	Concurrent use contraindicated
CYP1A2 inducers	Increased olanzapine metabolism reduces olanzapine effectiveness	Consider dose increases of olanzapine
CYP1A2 inhibitors	Decreased olanzapine metabolism increases risk of olanzapine toxicity	Consider dose decreases of olanzapine
QTc-prolonging agents	May increase the QTc interval	Avoid combining olanzapine with other agents that prolong the QTc interval

Adverse Reactions: Olanzapine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Akathisia, asthenia, dizziness, hypercholesterolemia, hyperglycemia, increased appetite, increased prolactin levels, increased triglycerides, somnolence, tremor, weight gain, xerostomia	Constipation, orthostatic hypotension, peripheral edema, personality disorder	Neuroleptic malignant syndrome, pancreatitis, sudden cardiac death, suicidal thoughts, tardive dyskinesia

Efficacy Monitoring Parameters. Improvement in schizophrenia, bipolar disorder, agitation, or treatment-resistant depression.

Toxicity Monitoring Parameters. FBG/HbA_{1c} prior to treatment and periodically in patients with DM. CBC, lipid profiles at baseline and periodically thereafter. Check body weight and BMI regularly during treatment. LFTs and electrolytes. Symptoms of neuroleptic malignant syndrome and involuntary movements/parkinsonian signs.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Drug may impair heat regulation. Rise from a sitting/lying-down position slowly. Report symptoms of tardive dyskinesia or neuroleptic malignant syndrome. Diabetic patients should monitor for hyperglycemia and report difficulties with glycemic control. Avoid alcohol while taking this drug.

Clinical Pearls. *Max* dose is 20 mg/d. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. Although the causes of death in clinical trials were varied, most of the deaths were cardiovascular or infectious in nature. Also available as an extended-release IM injection, which is used after establishing tolerance with oral olanzapine.

OLMESARTAN: Benicar

Daichi-Sankyo 40 mg pictured

Class: Angiotensin II Receptor Antagonist

Dosage Forms. **Oral Tablet:** 5 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypertension: Adults, 20 mg po daily, may titrate to 40 mg po daily; Children 6-16 y of age weighing 20-34 kg, 10 mg po daily, may titrate to 20 mg po daily; Children 6-16 y of age weighing >35 kg, 20 mg po daily, may titrate to 40 mg po daily

Off-Label Uses. None

MOA. Olmesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1).

Drug Characteristics: Olmesartan

Dose Adjustment Hepatic	Not required	**Absorption**	F = 26%, food has no effect on absorption
Dose Adjustment Renal	Not required, use with caution with CrCl <20 mL/min	**Distribution**	Vd = 17 L; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Intestinal wall; not via CYP
Pregnancy Category	D	**Elimination**	Renal elimination is 35-50% with a half-life of 3 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to olmesartan or other ARB, pregnancy, concurrent use with aliskiren in patients with DM	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Olmesartan

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Mevacor	No

Drug Interactions: Olmesartan

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
ACE-Is	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Eplerenone	Increased risk of hyperkalemia	Avoid concurrent use or monitor serum potassium levels
Potassium supplements	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive and natriuretic effect of olmesartan, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr level
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP
Aliskiren	Increased risk of hyperkalemia, hypotension, nephrotoxicity	Avoid use in with GFR <60 mL/min; monitor K, SCr, and BP

Adverse Reactions: Olmesartan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Back pain, dizziness, headache, hyperkalemia, hypotension	Angioedema, birth defects, hepatotoxicity, rhabdomyolysis, acute renal failure

Efficacy Monitoring Parameters. Decreased BP.

Toxicity Monitoring Parameters. Report signs/symptoms of hypotension. Baseline and periodic potassium, SCr, prior to initiating therapy and periodically thereafter.

Key Patient Counseling Points. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek care if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs. May cause orthostatic hypotension.

Clinical Pearls. ARBs can cause injury or death to the developing fetus; therapy should be stopped as soon as possible if pregnancy is detected.

OLOPATADINE: Patanol, Pataday

Class: Ophthalmic Antihistamine

Dosage Forms. Ophthalmic Solution: 0.1%, 0.2%

Common FDA Label Indication, Dosing, and Titration.

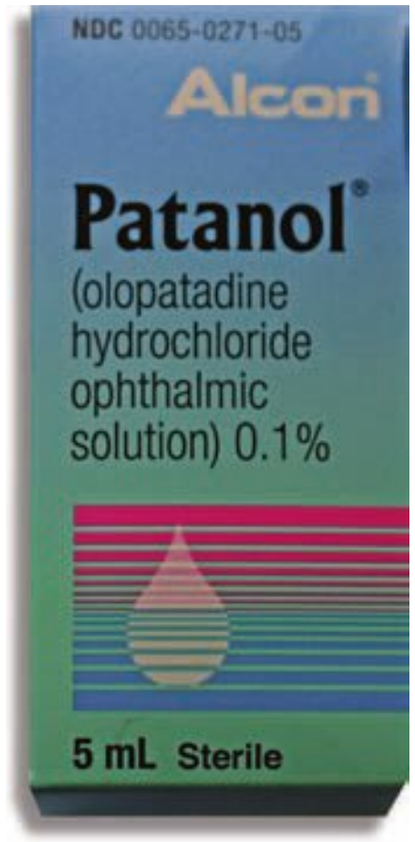
1. Allergic conjunctivitis: 1 drop of 0.1% solution in affected eye bid or 1 drop of 0.2% solution in affected eyes daily

Off-Label Uses. None

MOA. Olopatadine hydrochloride is a relatively selective histamine H_1-antagonist that exerts its effect by inhibiting the release of histamine from mast cells. It also blocks the type 1 immediate hypersensitivity reactions, including prevention of histamine-mediated effects on human conjunctival epithelial cells. It has no activity on dopamine, α-adrenergic, and muscarinic type 1 and type 2 receptors.

Drug Characteristics: Olopatadine

Dose Adjustment Hepatic	Not required	**Absorption**	Not measurable after ocular instillation
Dose Adjustment Renal	Not required	**Distribution**	Not measurable after ocular instillation
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to olopatadine	**Black Box Warnings**	None



Alcon 0.1% solution pictured

Medication Safety Issues: Olopatadine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Platinol	No

Drug Interactions: Olopatadine. None known

Adverse Reactions: Olopatadine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Taste sense altered, unpleasant taste in mouth, burning sensation in eye, keratitis, xerophthalmia, pharyngitis, cold syndrome, headache, nausea	Hypersensitivity reaction

Efficacy Monitoring Parameters. Reduction in ocular redness, itching, and irritation.

Toxicity Monitoring Parameters. Signs of hypersensitivity.

Key Patient Counseling Points. Wash hands. For administration, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on the bottle right away. Twice-daily dosing should be at least 6-8 h apart. Remove contact lens prior to administration and wait at least 10 min before reinserting. Do not use contact lenses if eyes are red.

Clinical Pearls. Not for use to treat contact lens-related irritation. Efficacy and safety established for patients ≥3 y of age. Also available in nasal formulation for seasonal allergic rhinitis.

OMEGA-3-ACID ETHYL ESTERS: Lovaza, Various

Class: Antihyperlipidemic, Omega-3 Fatty Acids

Dosage Forms. **Oral Capsule, Liquid Filled:** 1 g

Common FDA Label Indication, Dosing, and Titration.

1. Hypertriglyceridemia, adjunct to diet in adults with triglyceride levels 500 mg/dL or higher: 4 g po daily or divided into 2 doses

Off-Label Uses.

1. Coronary arteriosclerosis, hypertriglyceridemia: 4 g po daily or divided into 2 doses
2. Familial combined hyperlipidemia: 4 g po daily or divided into 2 doses
3. Heart failure: 4 g po daily or divided into 2 doses
4. Hyperlipidemia, hypertriglyceridemia, triglyceride levels <500 mg/dL: 4 g po daily or divided into 2 doses

GlaxoSmithKline 1 g pictured

MOA. Potential mechanisms of action include inhibition of acyl-CoA:1,2-diacylglycerol acyltransferase, increased mitochondrial and peroxisomal β-oxidation in the liver, decreased lipogenesis in the liver, and increased plasma lipoprotein lipase activity. Lovaza may reduce the synthesis of triglycerides in the liver because eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are poor substrates for the enzymes responsible for TG synthesis, and EPA and DHA inhibit esterification of other fatty acids.

Drug Characteristics: Omega-3-Acid Ethyl Esters

Dose Adjustment Hepatic	Not required	**Absorption**	Unknown
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Unknown	**Metabolism**	Oxidized in the liver similar to fatty acids derived from dietary sources; EPA: minor via CYP450
Pregnancy Category	C	**Elimination**	Half-life: EPA: ~37-89 h, DHA: ~46 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to omega-3–acid ethyl esters, f sh, or shellf sh	**Black Box Warnings**	None

Medication Safety Issues: Omega-3-Acid Ethyl Esters

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Liquid capsules	No	LORazepam	No

Drug Interactions: Omega-3-Acid Ethyl Esters. None known

Adverse Reactions: Omega-3–Acid Ethyl Esters

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Indigestion, taste alterations, rash, burping, diarrhea, arthralgia	Anaphylaxis, elevated LFTs

Efficacy Monitoring Parameters. Reduction in triglyceride levels.

Toxicity Monitoring Parameters. LDL, LFTs.

Key Patient Counseling Points. Swallow the whole capsule; take with food. Seek medical attention if severe rash, chest pain, heart palpitations, or shortness of breath.

Clinical Pearls. Omega-3–acid ethyl esters are available OTC as fish oil and contain lower amounts of DHA and EPA than the prescription version. OTC products have varying amounts of DHA and EPA. Each Lovaza capsule contains ~375 mg of DHA and 465 mg of EPA. Treatment of hypertriglyceridemia with omega-3–acid ethyl esters has shown to be equivalent to gemfibrozil in efficacy. Omega-3–acid ethyl esters have not been shown to decrease cardiovascular mortality.

OMEPRAZOLE: Prilosec, Various

Class: Proton Pump Inhibitor

Dosage Forms. Oral Capsule, Delayed Release: 10 mg, 20 mg, 40 mg; **Oral Tablet, Delayed Release:** 20 mg; **Oral Suspension:** 2 mg/mL; **Oral Packet:** 2.5 mg, 10 mg

Kremers Urban generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Duodenal ulcer disease: 20 mg po daily × up to 4 wk
2. Gastric ulcer disease: 40 mg po daily × up to 8 wk
3. *H. pylori* GI infection: 20 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
4. Erosive esophagitis, GERD: Adults and Children ≥1 y of age and ≥20 kg, 20 mg po daily; Children ≥1 y of age, 5-10 kg, 5 mg po daily; Children ≥1 y of age, 10-20 kg, 10 mg po daily

Off-Label Uses.

1. Drug-induced GI disturbance, indigestion: 20-40 mg po daily

MOA. Omeprazole is a PPI that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^+/K^+-ATPase (proton pump), which is the final pathway for acid secretion. Produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, and pentagastrin- and food-stimulated gastric acid secretion.

Drug Characteristics: Omeprazole

Dose Adjustment Hepatic	Consider dose adjustment in hepatic failure	**Absorption**	F = 30-40%, food delays but does not reduce absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.34-0.37 L/kg; 95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2C19 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 77% with a half-life of 30-60 min
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	CYP2C19 poor metabolizers have greater gastric acid suppression
Contraindications	Hypersensitivity to omeprazole or esomeprazole	**Black Box Warnings**	None

Medication Safety Issues: Omeprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
OTC	PriLOSEC	ER capsules and tablets	No	Plendil, Prevacid, PROzac	No

Drug Interactions: Omeprazole

Typical Agents	Mechanism	Clinical Management
Clopidogrel	Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness	Avoid concurrent use
CYP2C19 inhibitors	Decreased omeprazole metabolism increases risk of omeprazole toxicity	Consider dose decreases of omeprazole
CYP2C19 inducers	Increased omeprazole metabolism reduces omeprazole effectiveness	Consider dose increases of omeprazole
pH-dependent drugs	Lower gastric pH reduces absorption	Avoid concurrent use
Warfarin	Increased anticoagulant effect	Monitor INR and adjust warfarin dose accordingly

Adverse Reactions: Omeprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, diarrhea, headache	Toxic epidermal necrolysis, *C. diff cle* diarrhea, pancreatitis, hepatotoxicity, hip fracture, rhabdomyolysis, acute interstitial nephritis

Efficacy Monitoring Parameters. Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

Toxicity Monitoring Parameters. Severe headache or blistering skin rash. Seek medical attention for signs of liver failure, elevated LFTs.

Key Patient Counseling Points. Should be taken 1 h before meals.

Clinical Pearls. Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; patients should complete full regimen if prescribed for *H. pylori* management. Many PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of fractures, especially in elderly. Use lowest effective dose for those at risk for osteoporosis. Medication guide required at dispensing.

ONDANSETRON: Zofran, Various

Class: Antiemetic

Dosage Forms. **Oral Tablet:** 4 mg, 8 mg, 24 mg; **Oral Dispersible Tablet:** 4 mg, 8 mg; **Oral Solution:** 4 mg/5 mL; **Oral Film:** 4 mg, 8 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Chemotherapy-induced nausea and vomiting, highly emetogenic chemotherapy: 24 mg po 30 min prior to the start of chemotherapy
2. Chemotherapy-induced nausea and vomiting, moderately emetogenic chemotherapy: Adults and Children >12 y of age, 8 mg po 30 min prior to chemotherapy and repeated in 8 h, then 8 mg po q12h for 1-2 d post chemotherapy; Children 4-11 y of age, 4 mg po 30 min prior to chemotherapy, repeated 4 and 8 h after the 1st dose, then q8h for 1-2 d postchemotherapy
3. Prevention of postoperative nausea and vomiting: 16 mg po 1 h before anesthesia induction
4. Radiation-induced nausea and vomiting: 8 mg po 1-2 h prior to radiotherapy and q8h after 1st dose of radiation on each day of radiotherapy

Off-Label Uses.

1. Severe hyperemesis associated with pregnancy: 8 mg po q12h

MOA. Ondansetron is a selective 5-HT_3 receptor antagonist. Serotonin receptors of the 5-HT_3 type are present both peripherally and centrally in the chemoreceptor trigger zone. Cytotoxic chemotherapy releases serotonin from the enterochromaffin cells of the small intestine, initiating the vomiting reflex.

Drug Characteristics: Ondansetron

Dose Adjustment Hepatic	Severe hepatic dysfunction, *max* daily dose 8 mg	**Absorption**	F = 56%, food has minimal effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.5 L/kg
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal 5%, with a half-life of 4.6 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ondansetron, concurrent apomorphine or drugs that increase QT interval	**Black Box Warnings**	None

Medication Safety Issues: Ondansetron

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ODT	No	Film and disintegrating tablet	No	Zantac, Zosyn	No

Drug Interactions: Ondansetron

Typical Agents	Mechanism	Clinical Management
Apomorphine	Additive hypotension	Contraindicated
Agents that increase QT interval	Increased risk of QT prolongation (torsades de pointes, cardiac arrest)	Contraindicated
Cyclophosphamide	Ondansetron decreases the systemic exposure of cyclophosphamide	Avoid concurrent use

Adverse Reactions: Ondansetron

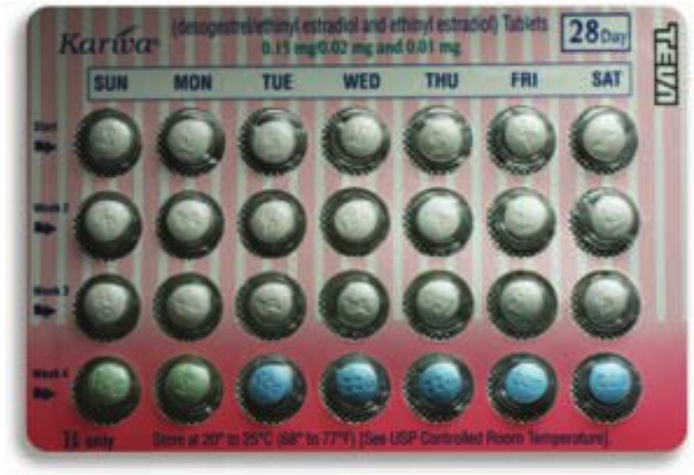
Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, diarrhea, headache	Xerostomia, increased LFTs, dizziness, fever	Arrhythmias, anaphylaxis, serotonin syndrome

Efficacy Monitoring Parameters. Reduction in nausea and vomiting.

Toxicity Monitoring Parameters. Heart palpitations, shortness of breath, severe rash.

Key Patient Counseling Points. Dry hands before handling disintegrating tablet. Do not open the blister pack that contains the tablet until you are ready to take it. Do not push the oral disintegrating tablet through the foil. Place tablet in mouth, allow to melt, swallow, or drink water.

Clinical Pearls. Tablets, disintegrating tablets, and solution are bioequivalent and are dosed interchangeably. 5-HT_3 receptor antagonists are often combined with dexamethasone and aprepitant for the prevention of chemotherapy-induced nausea/vomiting. Also available in injectable formulation.



Kariva by Teva pictured

Class: Oral Contraceptive

Product Contents: Oral Contraceptive—Biphasic

Phase 1 Content	Phase 2 Content	Example Brand Names
Ethinyl estradiol 20 mcg; desogestrel 0.15 mg (21 d)	Ethinyl estradiol 10 mcg (5 d)	Kariva, Azurette, Mircette
Ethinyl estradiol 20 mcg; levonorgestrel 0.1 mg (84 d)	Ethinyl estradiol 10 mcg (7 d)	LoSeasonique, Amethia Lo
Ethinyl estradiol 30 mcg; levonorgestrel 0.15 mg (84 d)	Ethinyl estradiol 10 mcg (7 d)	Seasonique, Amethia
Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (10 d)	Ethinyl estradiol 35 mcg; norethindrone 1 mg (11 d)	Necon 10/11
Ethinyl estradiol 10 mcg; norethindrone 1 mg (24 d)	Ethinyl estradiol 10 mcg (2 d)	Lo Loestrin Fe

Dosage Forms. **Oral Tablet:** Biphasic products contain 2 sets of tablets, each phase containing a combination of varying doses of estrogen/progestin agents, or an estrogen agent alone; products are either in 28-d or in 90-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate

Common FDA Label Indication, Dosing, and Titration.

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser

Off-Label Uses. None

MOA. See Preface C Card: General Content Related to All Oral Contraceptives.

Drug Characteristics: Oral Contraceptive—Biphasic[a]

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40% for ethinyl estradiol; food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 45 L/kg for ethinyl estradiol; highly protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Renal elimination with a half-life of 24 h for ethinyl estradiol
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day	**Black Box Warnings**	Cigarette smokers >35 y old

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

Medication Safety Issues: Oral Contraceptive—Biphasic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Multiple product names	Avoid oral estrogen and topical patch

Drug Interactions and Adverse Reactions: Oral Contraceptive—Biphasic. See Preface C Card: General Content Related to All Oral Contraceptives.

Efficacy Monitoring Parameters. Lack of pregnancy.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam.

Key Patient Counseling Points. See Preface C Card: General Content Related to All Oral Contraceptives.

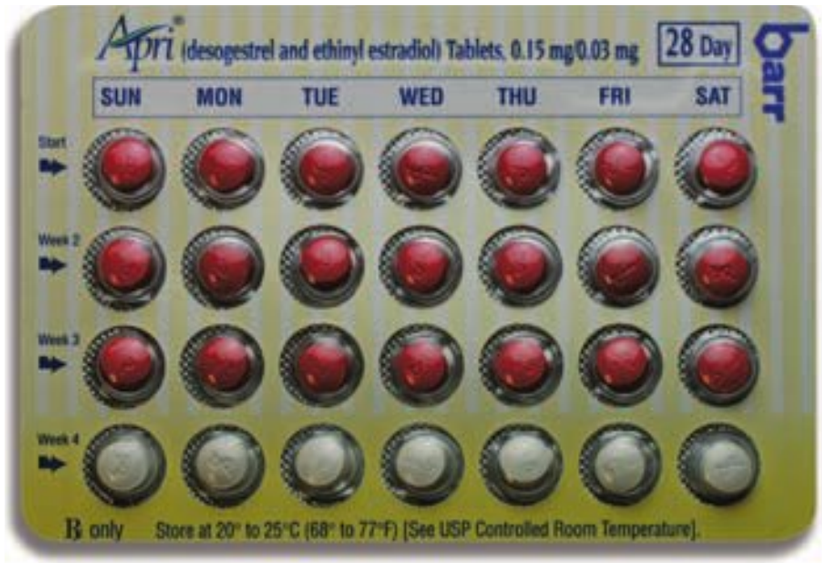
Clinical Pearls. Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian, and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

ORAL CONTRACEPTIVE—MONOPHASIC: Various

Class: Oral Contraceptive

Product Contents: Oral Contraceptive—Monophasic

Estrogen Component	Progestin Component	Example Brand Names
Ethinyl estradiol 50 mcg	Norgestrel 0.5 mg	Ogestrel 0.5/50
Ethinyl estradiol 35 mcg	Norethindrone 1 mg	Ortho-Novum 1/35, Norinyl 1 + 35
Ethinyl estradiol 35 mcg	Norethindrone 0.5 mg	Brevicon, Modicon
Ethinyl estradiol 35 mcg	Norethindrone 0.4 mg	Ovcon-35, Balziva
Ethinyl estradiol 35 mcg	Norethindrone 0.25 mg	MonoNessa, Ortho-Cyclen
Ethinyl estradiol 30 mcg	Drospirenone 3 mg	Ocella, Yasmin
Ethinyl estradiol 30 mcg	Norethindrone 1.5 mg	Loestrin 21 1.5/30
Ethinyl estradiol 30 mcg	Norgestrel 0.3 mg	Low-Ogestrel, Lo/Ovral
Ethinyl estradiol 30 mcg	Desogestrel 0.15 mg	Apri, Ortho-Cept
Ethinyl estradiol 30 mcg	Levonorgestrel 0.15 mg	Levora, Nordette-28
Ethinyl estradiol 20 mcg	Drospirenone 3 mg	Yaz, Loryna
Ethinyl estradiol 20 mcg	Levonorgestrel 0.1 mg	Aviane, Lutera
Ethinyl estradiol 20 mcg	Norethindrone 1 mg	Loestrin 21 1/20



Apri by Barr pictured

Dosage Forms. **Oral Tablet:** Monophasic products include tablets that each contains the same dose of an estrogen and progestin agent; products are either in 21-d or in 28-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate.

Common FDA Label Indication, Dosing, and Titration.

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser

Off-Label Uses. None

MOA. See Preface C Card: General Content Related to All Oral Contraceptives.

Drug Characteristics: Oral Contraceptive—Monophasic[a]

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40% for ethinyl estradiol; food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 45 L/kg for ethinyl estradiol; highly protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Renal elimination with a half-life of 24 h for ethinyl estradiol
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day	**Black Box Warnings**	Cigarette smokers >35 y old

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

Medication Safety Issues: Oral Contraceptive—Monophasic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Multiple product names	Avoid oral estrogen and topical patch

Drug Interactions and Adverse Reactions: Oral Contraceptive—Monophasic. See Preface C Card: General Content Related to All Oral Contraceptives.

Efficacy Monitoring Parameters. Lack of pregnancy.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam.

Key Patient Counseling Points. See Preface C Card: General Content Related to All Oral Contraceptives.

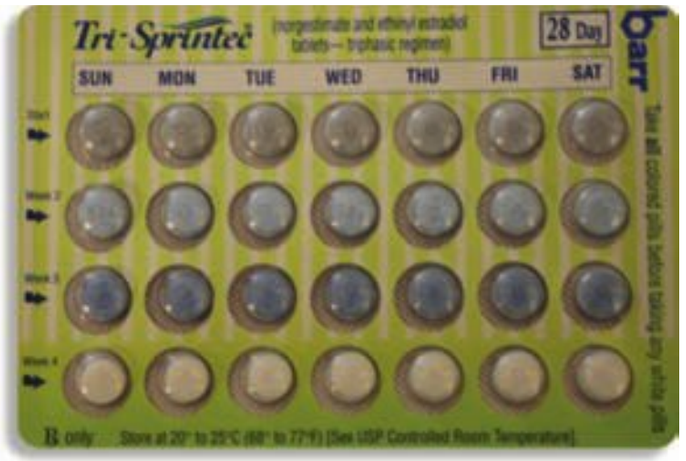
Clinical Pearls. Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian, and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

ORAL CONTRACEPTIVE—TRIPHASIC: Various

Class: Oral Contraceptive

Product Contents: Oral Contraceptive—Triphasic

Phase 1	Phase 2	Phase 3	Example Brand Names
Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (7 d)	Ethinyl estradiol 35 mcg; norethindrone 1 mg (9 d)	Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (5 d)	Tri-Norinyl, Aranelle
Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (7 d)	Ethinyl estradiol 35 mcg; norethindrone 0.75 mg (7 d)	Ethinyl estradiol 35 mcg; norethindrone 1 mg (7 d)	Ortho-Novum 7/7/7, Necon 7/7/7
Ethinyl estradiol 35 mcg; norgestimate 0.18 mg (7 d)	Ethinyl estradiol 35 mcg; norgestimate 0.215 mg (7 d)	Ethinyl estradiol 35 mcg; norgestimate 0.25 mg (7 d)	Ortho Tri-Cyclen, Tri-Sprintec, TriNessa
Ethinyl estradiol 25 mcg; norgestimate 0.18 mg (7 d)	Ethinyl estradiol 25 mcg; norgestimate 0.215 mg (7 d)	Ethinyl estradiol 25 mcg; norgestimate 0.25 mg (7 d)	Ortho Tri-Cyclen Lo
Ethinyl estradiol 20 mcg; norethindrone 1 mg (5 d)	Ethinyl estradiol 30 mcg; norethindrone 1 mg (7 d)	Ethinyl estradiol 35 mcg; norethindrone 1 mg (9 d)	Estrostep Fe, Tri-Legest



Tri-Sprintec by Barr pictured

Dosage Forms. **Oral Tablet:** Triphasic products contain 3 sets of tablets, each phase containing a combination of varying doses of estrogen/progestin agents; products are either in 21-d or in 28-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate.

Common FDA Label Indication, Dosing, and Titration.

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser
2. Acne vulgaris, moderate: In females at least 15 y of age who have achieved menarche and are unresponsive to topical antiacne medications, same dosing as for contraception (Ortho Tri-Cyclen and Estrostep Fe are the only products with this FDA-approved indication)

Off-Label Uses. None

MOA. See Preface C Card: General Content Related to All Oral Contraceptives.

Drug Characteristics: Oral Contraceptive—Triphasic[a]

Dose Adjustment Hepatic	Not required	**Absorption**	F = 40% for ethinyl estradiol; food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 45 L/kg for ethinyl estradiol; highly protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Renal elimination with a half-life of 24 h for ethinyl estradiol
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day	**Black Box Warnings**	Cigarette smokers >35 y old

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

Medication Safety Issues: Oral Contraceptive—Triphasic

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Multiple product names	Avoid oral estrogen and topical patch

Drug Interactions and Adverse Reactions: Oral Contraceptive—Triphasic. See Preface C Card: General Content Related to All Oral Contraceptives.

Efficacy Monitoring Parameters. Lack of pregnancy.

Toxicity Monitoring Parameters. Annual physical examination including cervical cytology (Pap smear) and breast exam.

Key Patient Counseling Points. See Preface C Card: General Content Related to All Oral Contraceptives.

Clinical Pearls. Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

OSELTAMIVIR: Tamiflu

Class: Neuraminidase Inhibitor, Antiviral

Dosage Forms. Oral Capsule: 30 mg, 45 mg, 75 mg; **Oral Suspension:** 6 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Influenza virus types A and B, treatment: Children >1 y of age and <15 kg, 30 mg po bid × 5 d; Children >1 y of age and 15-23 kg, 45 mg po bid × 5 d; Children >1 y of age and 23-40 kg, 60 mg po bid × 5 d; Adults and Children >1 y of age and >40 kg, 75 mg po bid × 5 d
2. Influenza virus types A and B, prophylaxis: Same dose as for treatment; may dose for 6 wk during a community outbreak

Off-Label Uses.

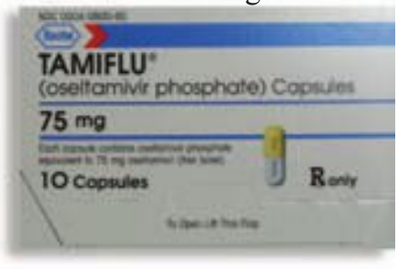
1. Influenza virus types A and B, prophylaxis: Children >2 wk and <3 mo of age, 3 mg/kg/d for up to 6 wk during community outbreak

MOA. Oseltamivir is an inhibitor of influenza virus neuraminidase affecting release of viral particles.

30 mg

45 mg

75 mg



Roche pictured

Drug Characteristics: Oseltamivir

Dose Adjustment Hepatic	Not required	**Absorption**	F = 75%, food has minimal effect on absorption
Dose Adjustment Renal	CrCl = 10-30 mL/min, reduce dose to 30 mg po daily for prophylaxis and 75 mg po daily × 5 d for treatment	**Distribution**	Vd = 23-26 L; 42% protein bound
Dialyzable	Yes	**Metabolism**	Oseltamivir phosphate is a prodrug that is extensively metabolized to oseltamivir carboxylate by ester hydrolysis
Pregnancy Category	C	**Elimination**	Renal elimination 99%, with a half-life of 1-3 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to oseltamivir	**Black Box Warnings**	None

Medication Safety Issues: Oseltamivir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Thera-Flu	No

Drug Interactions: Oseltamivir

Typical Agents	Mechanism	Clinical Management
Influenza vaccine (live)	Interferes with vaccine effectiveness	Vaccinate 2 wk before or 48 h after administration of oseltamivir

Adverse Reactions: Oseltamivir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, vomiting	Diarrhea, elevated LFTs	Arrhythmias, anaphylaxis, Stevens-Johnson syndrome, seizures, delirium

Efficacy Monitoring Parameters. Prevention or resolution of influenza infection symptoms.

Toxicity Monitoring Parameters. Seek care if heart palpitations, shortness of breath, severe rash, swelling, confusion, or anxiety occurs.

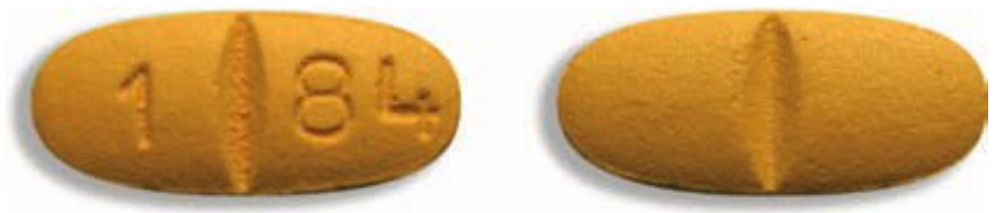
Key Patient Counseling Points. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek care. Suspension is available in a 6-mg/mL concentration and is packaged with an oral syringe calibrated in milliliters up to a total of 10 mL. Instructions to the patient should be provided based on these units of measure (ie, mL). When providing oseltamivir suspension for children <1 y of age, use a lower calibrated (ie, <10 mL) oral syringe to ensure accurate dosing. If suspension unavailable, open capsules and compound a 6-mg/mL suspension.

Clinical Pearls. Candidates for prophylaxis include close contacts of a confirmed or suspected case during their infectious period who are at high risk for influenza complications, health-care workers and emergency medical personnel, and pregnant women; treatment must start within 48 h of exposure. Capsules may be opened and administered in liquid or via nasogastric tube. Severely ill patients may require longer treatment.

OXCARBAZEPINE: Trileptal, Various

Class: Dibenzazepine Carboxamide, Anticonvulsant

Dosage Forms. Oral Tablet: 150 mg, 300 mg, 600 mg; **Oral Tablet, Extended Release:** 150 mg, 300 mg, 600 mg; **Oral Suspension:** 300 mg/5 mL



Sun Pharma generic 300 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Partial seizure: Adults, 300 mg po bid, may titrate to 1200 mg/d po; Children 4-16 y of age, 8-10 mg/kg/d po in 2 divided doses, may titrate to 600 mg/d po

Off-Label Uses.

1. Trigeminal neuralgia: 300 mg po bid-qid, may titrate to 2400 mg po daily

MOA. Oxcarbazepine is a 10-keto analogue of carbamazepine that exerts its anticonvulsant effect through an active 10-monohydroxy metabolite (MHD). Its mechanism of action is not known but likely involves blockade of voltage-dependent sodium channels and inhibition of repetitive neuronal firing.

Drug Characteristics: Oxcarbazepine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 100%, food has no effect on absorption
Dose Adjustment Renal	CrCl <30 mL/min, initiate at 300 mg/d and increase slowly	**Distribution**	Vd = 49 L; 40-60% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic metabolism, CYP3A4/5 substrate; inducer of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is >95% with a half-life of 8-13 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None
Contraindications	Hypersensitivity to oxcarbazepine	**Black Box Warnings**	None

Medication Safety Issues: Oxcarbazepine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	OXcarbazepine	Extended-release tablets	No	CarBAMazepine	No

Drug Interactions: Oxcarbazepine

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased oxcarbazepine metabolism reduces oxcarbazepine effectiveness	Consider dose increases of oxcarbazepine
CYP3A4/5 inhibitors	Decreased oxcarbazepine metabolism increases oxcarbazepine toxicity	Monitor and consider dose decreases of oxcarbazepine
CYP3A4/5 substrates	Oxcarbazepine increases metabolism of substrates drugs, lowers plasma concentration, and decreases substrate drug activity	Avoid concurrent use or monitor substrate drug and increase dose
Carbamazepine, phenobarbital, valproic acid, verapamil	Decreased oxcarbazepine concentrations	Monitor eff cacy of oxcarbazepine
Oral contraceptives	Decreased contraceptive eff cacy	Use an alternative form of birth control

Adverse Reactions: Oxcarbazepine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Somnolence, headache, diplopia, dizziness	Abnormal vision, anorexia, ataxia, constipation, diarrhea, drowsiness, fatigue, hyponatremia, nausea, rash, tremor, vomiting, weight gain	Anaphylaxis, angioedema, Stevens-Johnson syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Reduction in seizure frequency.

Toxicity Monitoring Parameters. Serum sodium during maintenance treatment, emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior.

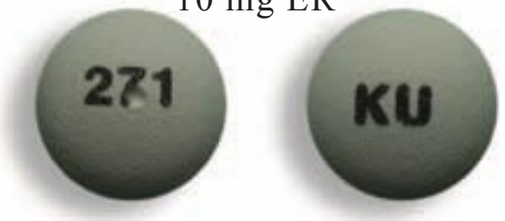
Key Patient Counseling Points. Suspension should be shaken well and dose prepared immediately using oral dosing syringe. Suspension can be mixed in a small glass of water just prior to administration or may be swallowed directly from the syringe. Avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient to report signs/symptoms of serious dermatologic reactions, myelosuppression, or hepatotoxicity. Take with food, but not alcohol, grapefruit, or grapefruit juice. Avoid abrupt discontinuation to avoid risk of seizure.

Clinical Pearls. Safety and efficacy not established in pediatric patients <4 y of age. With adjunctive therapy, children 2-4 y of age may require up to twice the oxcarbazepine dose per body weight compared to adults, and children 4-12 y of age may require a 50% higher oxcarbazepine dose per body weight compared to adults. Medication guide required at dispensing.

OXYBUTYNIN: Ditropan, Various

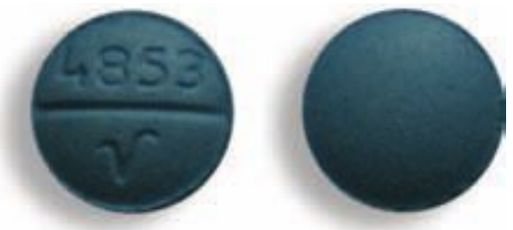
5 mg ER

10 mg ER



Kremers Urban generic ER pictured

5 mg
immediate release



Qualitest generic pictured

Class: Urinary Antispasmodic

Dosage Forms. **Oral Tablet:** 5 mg; **Oral Tablet, Extended Release:** 5 mg, 10 mg, 15 mg; **Oral Syrup:** 5 mg/5 mL; **Transdermal Gel**: 3%, 10%; **Transdermal Patch:** 3.9 mg/24 h

Common FDA Label Indication, Dosing, and Titration.

1. Overactive or neurogenic bladder: Oral, 5-10 mg/d po, may titrate to 30 mg/d po; Gel, 100 mg/g applied once daily; Patch, 1 patch applied twice weekly

Off-Label Uses. None

MOA. Oxybutynin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

Drug Characteristics: Oxybutynin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 6%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 193 L
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal with a half-life of 2-3 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to oxybutynin, gastric retention, glaucoma, urinary retention	**Black Box Warnings**	None

Medication Safety Issues: Oxybutynin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	No	Extended-release formulation	No	OxyCONTIN, Diprivan	No

Drug Interactions: Oxybutynin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inhibitors	Decreased oxybutynin metabolism increases risk of oxybutynin toxicity	Consider dose decreases of oxybutynin
CYP3A4/5 inducers	Increased oxybutynin metabolism decreases oxybutynin efficacy	Consider dose increases of oxybutynin
Anticholinergic agents	Additive anticholinergic adverse effects can occur	Avoid concurrent use or monitor carefully for adverse effects

Adverse Reactions: Oxybutynin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, xerostomia, blurred vision	Abdominal pain, dizziness, indigestion, urinary retention, arthralgias, hyperglycemia	Prolonged QTc interval, seizures, tachycardia

Efficacy Monitoring Parameters. Resolution of clinical signs of incontinence, urinary frequency, urinary urgency.

Toxicity Monitoring Parameters. Seek medical attention if anticholinergic effects (dry mouth, constipation, cognitive impairment, vision changes) are severe; monitor FBG, HR.

Key Patient Counseling Points. This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment.

Clinical Pearls. Patients should be advised to exercise caution in decisions to engage in potentially dangerous activities until the drug's effects have been determined. May note decline in cognitive function, especially in elderly. The transdermal patch is available OTC.

OXYCODONE: Oxycontin, Various

Class: Opioid Analgesic. C-II

Dosage Forms. **Oral Tablet, Immediate Release**: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg; **Oral Tablet, Extended Release:** 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg; **Oral Capsule:** 5 mg; **Oral Concentrate**: 100 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

1. Pain, chronic, moderate to severe: Extended release, 10-20 mg po q12h prn pain, may titrate to response; immediate release, 5-15 mg po q4-6h prn pain

Off-Label Uses. None

MOA. Oxycodone is pure mu agonist. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing the brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation. It also decreases gastric, biliary, and pancreatic secretion, induces peripheral vasodilation, and promotes opioid-induced hypotension due to histamine release.

Purdue Pharma pictured

Drug Characteristics: Oxycodone

Dose Adjustment Hepatic	Moderate impairment, reduce dose by 33%; severe impairment, reduce dose by 50%	**Absorption**	F = 60-87%; absorption enhanced by food
Dose Adjustment Renal	CrCl <60 mL/min, reduce starting dose	**Distribution**	Vd = 2.6 L/kg; 45% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal elimination is 20% with a half-life of 5 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to oxycodone or other opioids, asthma, paralytic ileus, respiratory depression, hypercarbia	**Black Box Warnings**	Abuse potential; do not crush ER tablet

Medication Safety Issues: Oxycodone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	OxyCODONE	Do not crush or chew ER or abuse deterrent formulation	Yes	HYDROcodone, MS Contin, oxybutynin	No

Drug Interactions: Oxycodone

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP3A4/5 inducers	Increased oxycodone metabolism decreases efficacy	Use with caution, consider increasing dose of oxycodone
CYP3A4/5 inhibitors	Decreased oxycodone metabolism increases risk of toxicity	Use with caution, consider decreasing dose of oxycodone

Adverse Reactions: Oxycodone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, GI distress, sedation, sweating, pruritus	Asthenia, dyspnea, hypotension, euphoria	Cardiac arrest, physical dependence, tolerance, severe hypersensitivity

Efficacy Monitoring Parameters. Relief of pain.

Toxicity Monitoring Parameters. Excessive drowsiness, severe skin rash, decreased breathing, severe constipation, chest pain, dizziness. Monitor vital signs, specifically respiratory rate and BP.

Key Patient Counseling Points. Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

Clinical Pearls. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Extended-release products must not be crushed or chewed. Crushing or chewing will release the total dose of oxycodone at once and increase risk of respiratory depression. Extended-release products are not for use in children. Advise patients to keep in safe place, and dispose of properly when no longer needed. Now in REMS program prescribers are required to receive appropriate training. Medication guide required when dispensing.

PANTOPRAZOLE: Protonix, Various

Class: Proton Pump Inhibitor

Dosage Forms. **Oral Tablet, Delayed Release:** 20 mg, 40 mg; **Oral Packet:** 40 mg

Teva generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Erosive esophagitis, GERD: Children ≥5 y of age and 15-40 kg, 20 mg po daily × up to 8 wk; Adults and Children ≥5 y of age and >40 kg, 40 mg po daily
2. Gastric hypersecretion: 40 mg po bid, may titrate to 240 mg/d po
3. Zollinger-Ellison syndrome: 40 mg po bid, may titrate to 240 mg/d po

Off-Label Uses.

1. *H. pylori* GI tract infection: 40 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
2. Duodenal ulcer disease: 40-80 mg po daily × up to 4-8 wk

MOA. Pantoprazole is a PPI that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^+/K^+-ATPase (proton pump), which is the final pathway for acid secretion. Produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, pentagastrin-stimulated, and food-stimulated gastric acid secretion.

Drug Characteristics: Pantoprazole

Dose Adjustment Hepatic	Not required	**Absorption**	F = 77%, food has no effect on absorption of delayed release tablet
Dose Adjustment Renal	Not required	**Distribution**	98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, substrate for CYP2C19
Pregnancy Category	B	**Elimination**	Renal elimination is 71% with a half-life of 1 h (10 h in CYP2C19-deficient patients)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Poor CYP2C19 metabolizers; if known, consider lower dose
Contraindications	Hypersensitivity to pantoprazole	**Black Box Warnings**	None

Medication Safety Issues: Pantoprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Delayed-release tablet, oral packet	No	ARIPiprazole	No

Drug Interactions: Pantoprazole

Typical Agents	Mechanism	Clinical Management
CYP2C19 inducers	Increased pantoprazole metabolism reduces pantoprazole effectiveness	Consider dose increases of pantoprazole
CYP2C19 inhibitors	Decreased pantoprazole metabolism increases risk of pantoprazole toxicity	Consider dose decreases of pantoprazole
Clopidogrel	Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness	Avoid concurrent use
Methotrexate	Pantoprazole blocks the active secretion of methotrexate, increasing methotrexate levels	Use with caution; monitor for signs of methotrexate toxicity
pH dependent drugs	Lower gastric pH reduces absorption	Monitor for lack of effectiveness of interacting drug and adjust dose as necessary

Adverse Reactions: Pantoprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, diarrhea, f atulence, headache	Toxic epidermal necrolysis, Stevens-Johnson syndrome, thrombocytopenia, hip fracture, rhabdomyolysis, acute interstitial nephritis

Efficacy Monitoring Parameters. Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

Toxicity Monitoring Parameters. Seek medical care for severe headache or blistering skin rash.

Key Patient Counseling Points. Can be taken with or without food but best if taken before meals to reduce acid production caused by food.

Clinical Pearls. When the intravenous route is used, converted to oral route as soon as possible to avoid cost and risks of intravenous therapy. Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; counsel patient to complete full regimen if prescribed for *H. pylori* management. Other PPI and H_2 antagonists are available OTC; do not take multiple products concurrently to avoid additive risk of adverse effects. Also available as IV formulation. Packet formulation is delayed release; sprinkle into apple sauce or apple juice only, swallow immediately.

PAROXETINE: Paxil, Paxil CR, Various

Class: SSRI Antidepressant

Dosage Forms. Oral Tablet: 10 mg, 20 mg, 30 mg, 40 mg; **Oral Tablet, Controlled Release:** 12.5 mg, 25 mg, 37.5 mg; **Oral Solution, Oral Syrup:** 10 mg/5 mL; **Oral Suspension:** 10 mg/5 mL; **Oral Capsule:** 7.5 mg

Aurobindo generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Adults, immediate release, 20 mg po daily, may titrate to 50 mg po daily; Adults, controlled release, 25 mg po daily, may titrate to 62.5 mg po daily; Children ≥8 y of age, 10-20 mg po daily
2. Generalized anxiety disorder: Adults, 20 mg po daily
3. Social anxiety disorder: Adults, 20 mg po daily; Children ≥8 y of age, 10 mg po daily
4. OCD: Adults, 20 mg po daily, titrate to 60 mg po daily; Children ≥8 y of age, 10 mg po daily, may titrate to 30 mg daily
5. Panic disorder: Immediate release, 10 mg po daily, may titrate to 60 mg po daily; controlled release, 12.5 mg po daily, may titrate to 75 mg po daily
6. Posttraumatic stress disorder (PTSD): Adults, 20 mg po daily, may titrate to 50 mg po daily
7. Premenstrual dysphoric disorder (PMDD): 12.5 mg po daily or × 14 d prior to expected start of menses, may titrate to 25 mg po daily
8. Vasomotor symptoms of menopause: 7.5 mg po daily at bedtime

Off-Label Uses. None

MOA. Paroxetine is a highly selective and potent inhibitor of serotonin reuptake (SSRI).

Drug Characteristics: Paroxetine

Dose Adjustment Hepatic	*Max* dose 40 mg immediate release, or 50 mg controlled release	**Absorption**	F = 100%, food increases Cmax and AUC
Dose Adjustment Renal	*Max* dose 40 mg immediate release, or 50 mg controlled release	**Distribution**	93-95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2D6 substrate
Pregnancy Category	D	**Elimination**	Renal elimination is 64% with a half-life of 15-22 h
Lactation	Avoid	**Pharmacogenetics**	Use with caution in CYP2D6 poor metabolizers
Contraindications	Hypersensitivity to paroxetine; concomitant use of thioridazine or MAOIs	**Black Box Warnings**	Suicidality

Medication Safety Issues: Paroxetine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CR	PARoxetine	CR or film-coated product	No	Doxil, Plavix, PROzac, FLUoxetine	No

Drug Interactions: Paroxetine

Typical Agents	Mechanism	Clinical Management
CYP2D6 inhibitors	Decreased paroxetine metabolism increases risk of paroxetine toxicity	Consider dose decreases of paroxetine
Antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Triptans, dextroamphetamine, tramadol, linezolid, MAOIs	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome; linezolid, MAOIs contraindicated
Clozapine	Increased clozapine concentrations	Monitor for adverse effects
Agents that increase QT interval	Increased risk of QT prolongation (torsades de pointes, cardiac arrest)	Avoid concurrent use or monitor carefully

Adverse Reactions: Paroxetine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Abnormal ejaculation, asthenia, constipation, diarrhea, headache, insomnia, nausea, somnolence	Anxiety, asthenia, bleeding, dizziness, diaphoresis, feeling nervous, impotence, insomnia, loss of appetite, rash, reduced libido, tremor, vomiting, xerostomia	Serotonin syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression, panic disorder, OCD, premenstrual syndrome, vasomotor symptoms.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

Key Patient Counseling Points. Do not chew or crush controlled-release tablet or film-coated tablet (Pexeva). Shake suspension well before using. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Avoid abrupt discontinuation. Do not drink alcohol. Use caution with NSAIDs or aspirin while taking this drug.

Clinical Pearls. If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate.

PENICILLIN: Various

Class: Antibiotic

Dosage Forms. **Oral Tablet:** 250 mg, 500 mg; **Oral Solution:** 125 mg/5 mL, 250 mg/5 mL

Sandoz generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Bacterial endocarditis, prophylaxis in patients with congenital heart disease or rheumatic/acquired valvular heart disease: Adults, 2 g po 1 h prior to procedure and then 1 g po 6 h later; Children <60 lb, 1 g po 1 h prior to procedure and then 500 mg po 6 h later
2. Otitis media, mild-moderate, pneumococcal: Adults, 250-500 mg po q6h until afebrile for at least 2 d; Children <12 y of age, 25-50 mg/kg/d po in 3-4 divided doses, *max* 3 g/d
3. Streptococcal pharyngitis: Adults, 500 mg po bid × 10 d; Children <60 lb, 250 mg po bid × 10 d

Off-Label Uses.

1. Pneumococcal infectious disease, prophylaxis in patients with sickle cell disease or asplenia: Children 2 mo to 5 y of age, 125 mg po bid; Children ≥5 y of age, 250 mg po bid; discontinue at age 5 y for children who received pneumococcal vaccination and who have not experienced invasive pneumococcal disease

MOA. Penicillins are active against most gram-positive organisms and some gram-negative organisms, notably *Neisseria* spp., by interfering with late stages of bacterial cell wall synthesis; resistance is caused primarily by bacterial production of β-lactamases; some organisms have altered penicillin-binding protein targets (eg, *Enterococci* spp. and *S. pneumoniae*); others have impermeable outer cell wall layers.

Drug Characteristics: Penicillin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 25%, food delays but does not reduce absorption
Dose Adjustment Renal	Not required	**Distribution**	Pericardium, pleural f uid, and inner ear
Dialyzable	Unknown	**Metabolism**	Not metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 20-40% with a half-life of 30 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to penicillins	**Black Box Warnings**	None

Medication Safety Issues: Penicillin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Penicillin G	No

Drug Interactions: Penicillin

Typical Agents	Mechanism	Clinical Management
Probenecid	Increases serum concentration of penicillin	Avoid concurrent use
Tetracyclines	Decreased effectiveness of penicillins	Avoid concurrent use

Adverse Reactions: Penicillin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea	Skin rash	Severe hypersensitivity, renal failure, hepatic failure, hemolytic anemia

Efficacy Monitoring Parameters. Resolution of clinical signs of infection.

Toxicity Monitoring Parameters. Seek care for severe diarrhea, dark urine, yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Assess SCr and CBC if prolonged therapy.

Key Patient Counseling Points. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek medical care. Take on an empty stomach.

Clinical Pearls. There is cross-hypersensitivity between penicillin and cephalosporins (<10%); use with caution in cephalosporin allergy if severe penicillin reaction. May resume normal activities after 24 h of antibiotics if afebrile. First antibiotic, produced in 1943, referred to as the "magic bullet." Aminopenicillins have replaced use of penicillin for many indications, including endocarditis and otitis media.

PENTOSAN: Elmiron

Class: Urinary Analgesic

Dosage Forms: Oral Capsule: 100 mg

Common FDA Label Indication, Dosing, and Titration.

1. Pain relief from interstitial nephritis: 100 mg po tid

Off-Label Uses. None

MOA. Pentosan is a low-molecular-weight heparin-like compound. The mechanism of action of pentosan in relieving pain associated with interstitial cystitis is not known, but it has been found to adhere to the mucosal membrane of the bladder wall and may act as a buffer to control cell permeability, which prevents irritating solutes in urine from reaching the cells.

Janssen 100 mg pictured

Drug Characteristics: Pentosan

Dose Adjustment Hepatic	Not required	**Absorption**	F = 6%
Dose Adjustment Renal	Not required	**Distribution**	Uroepithelium of genitourinary tract
Dialyzable	Not known	**Metabolism**	Metabolized in liver and spleen via desulfation
Pregnancy Category	B	**Elimination**	Majority of dose eliminated unchanged in feces with half-life of 20-27 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	None	**Black Box Warnings**	None

Medication Safety Issues: Pentosan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Imuran, pentostatin	No

Drug Interactions: Pentosan

Typical Agents	Mechanism	Clinical Management
Antiplatelet agents, NSAIDs, and anticoagulants	Additive risk of bleeding	Use with caution and monitor carefully

Adverse Reactions: Pentosan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Alopecia, rash, diarrhea, nausea, dizziness, headache, ecchymosis, epistaxis, gum bleeding	Rectal hemorrhage, thrombocytopenia

Efficacy Monitoring Parameters. Resolution of signs and symptoms of interstitial nephritis, including nocturia, urinary pain, urinary frequency, or urinary urgency.

Toxicity Monitoring Parameters. Monitor for bleeding complications.

Key Patient Counseling Points. Take 1 h before or 2 h after meals. Use caution and monitor for bleeding if using concomitant NSAIDs or aspirin-containing products.

Clinical Pearls. Patients should be evaluated after 3 mo, and if treatment has not provided benefit, a 2nd 3-mo trial may be attempted (provided no adverse effects have occurred). If the patient does not respond after 6 mo, the product is not likely to provide benefit.

PERTUSSIS VACCINE, ACELLULAR: Daptacel, Adacel, Boostrix

Class: Vaccine

Dosage Forms. **Suspension for Intramuscular Injection:** For Adults, available in combination with tetanus and diphtheria toxoids (Tdap); for Children, available in combination with diphtheria and tetanus toxoids (DTaP), and in combination with other pediatric vaccines

Infanrix, GlaxoSmithKline pictured

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of pertussis: Children, all infants at age 2, 4, 6, and 12-15 mo, and a 5th dose at age 4-6 y, as primary series of DTaP; Tdap at age 11-12 y; single dose of Tdap for all adults at next opportunity

Off-Label Uses.

1. Prevention of pertussis during pregnancy and in early infancy: Pregnant females, preferably during 27-36 wk gestation of each pregnancy, Tdap.

Drug Characteristics: Pertussis Vaccine, Acellular

Pregnancy Category	C	**ADME**	None known
Lactation	Caution advised; weigh risk and benefit	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to pertussis vaccine or a component of the vaccine; Encephalopathy without known cause within 7 d of a pertussis containing vaccine	**Black Box Warnings**	None

Medication Safety Issues: Pertussis Vaccine, Acellular

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names
No	No	No	No	Adacel, Daptacel

Drug Interactions: Pertussis Vaccine, Acellular

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression reduces vaccine efficacy	Delay pertussis vaccine administration until corticosteroid therapy has been discontinued if possible
Immunosuppressing agents	Immunosuppression reduces vaccine efficacy	Delay pertussis vaccine administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: Pertussis Vaccine, Acellular

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb	GI symptoms	Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of pertussis.

Toxicity Monitoring Parameters. Monitor for syncope, fever after administration.

Key Patient Counseling Points. Return to provider for each dose in the series.

Clinical Pearls. Use the same brand of vaccine to complete the entire series, if possible. Adacel not for use in children <11 y of age. Daptacel not for use in children <6 wk or >6 y of age. Use caution to avoid mistaking Tdap and DTaP products.

PHENAZOPYRIDINE: Pyridium, Various

Class: Urinary Tract Analgesic

Dosage Forms. Oral Tablet: 95 mg, 97.2 mg, 100 mg, 200 mg

Common FDA Label Indication, Dosing, and Titration.

1. Dysuria (pain, burning, and other discomforts of the lower urinary tract caused by infection, trauma, surgery, endoscopic procedures, or the passage of catheters): 100-200 mg po tid after meals; should not be used for >2 d when administered in conjunction with an antibiotic

Off-Label Uses. None

MOA. Phenazopyridine is excreted in the urine where it exerts a topical analgesic effect on the mucosa of the urinary tract. This action helps relieve pain, burning, urgency, and frequency. The precise mechanism of action is not known.

Breckenridge generic
100 mg pictured

Drug Characteristics: Phenazopyridine

Dose Adjustment Hepatic	Not required	**Absorption**	Not known
Dose Adjustment Renal	CrCl <50 mL/min, avoid	**Distribution**	Not known
Dialyzable	Unknown	**Metabolism**	Some hepatic metabolism
Pregnancy Category	B	**Elimination**	Renal elimination is 66%
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to phenazopyridine, renal failure	**Black Box Warnings**	None

Medication Safety Issues: Phenazopyridine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Phenoxybenzamine, pyridoxine	No

Drug Interactions: Phenazopyridine. None known

Adverse Reactions: Phenazopyridine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Headache, rash, pruritus, GI upset	Anaphylaxis, methemoglobinemia, hemolytic anemia, hepatotoxicity, nephrotoxicity

Efficacy Monitoring Parameters. Resolution of clinical symptoms of dysuria (painful urination).

Toxicity Monitoring Parameters. Signs of hemolytic anemia, hepatotoxicity, or nephrotoxicity.

Key Patient Counseling Points. Drug may discolor urine and sclera to red or orange, causing staining of undergarments and contact lenses. Patient should take drug with food to minimize gastric irritation.

Clinical Pearls. When used in the treatment of a urinary tract infection, phenazopyridine should not exceed 2 d because there is a lack of evidence that the combined administration of phenazopyridine and an antibacterial provides greater benefit than administration of the antibacterial alone after 2 d. Many OTC products containing phenazopyridine are also available.

PHENOBARBITAL: Luminal, Various

Class: Long-Acting Barbiturate. C-IV

Dosage Forms. Oral Tablet: 15 mg, 16.2 mg, 30 mg, 32.4 mg, 60 mg, 64.8 mg, 97.2 mg, 100 mg; **Oral Elixir, Oral Solution:** 20 mg/5 mL

Excellium generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Epilepsy: Adults, 50-100 mg po bid-tid; Children, 15-50 mg po bid-tid (tablet) or 3-6 mg/kg/d po (solution)
2. Daytime sedation: Adults, 30-120 mg po divided into 2-3 doses, may titrate to 400 mg/d; Children, 6 mg/kg/d po divided into 3 doses

Off-Label Uses.

1. Sleep: Adults, 100-320 mg po as single dose.

MOA. Phenobarbital produces different degrees of depression within the CNS, from sedation to general anesthesia. It has been demonstrated to depress monosynaptic responses in the CNS only transiently, but synaptic recovery is delayed and a decrease in postsynaptic resistance is observed at some synapses.

Drug Characteristics: Phenobarbital

Dose Adjustment Hepatic	Dosage reduction recommended	**Absorption**	F = 80-100%, food has no effect on absorption
Dose Adjustment Renal	CrCl <10 mL/min, extend dosing interval to q12-16h	**Distribution**	Vd = 0.5-1 L/kg; 20-60% protein bound
Dialyzable	Yes	**Metabolism**	Hepatic, CYP2C19 substrate; strong inducer of CYP1A2, 2A6, 2B6, 2C8, 2C9, and 3A4/5
Pregnancy Category	D	**Elimination**	Renal elimination is 21% with a half-life of 1.5-4.9 d
Lactation	Compatible, monitor infant for side effects	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to barbiturates; marked liver function impairment; respiratory disease with evidence of dyspnea or obstruction; history of sedative or hypnotic addiction; personal or family history of acute intermittent porphyria	**Black Box Warnings**	None

Medication Safety Issues: Phenobarbital

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	PHENobarbital	No	No	PENTobarbital, Phenergan	Avoid

Drug Interactions: Phenobarbital

Typical Agents	Mechanism	Clinical Management
Substrates of CYP1A2, 2A6, 2B6, 2C8, 2C9, and 3A4/5	Increases metabolism of substrates, reducing effectiveness	Consider increasing dose of substrates
CYP2C19 inducers	Increased phenobarbital metabolism reduces phenobarbital effectiveness	Consider dose increases of phenobarbital
CYP2C19 inhibitors	Decreased phenobarbital metabolism increases risk of phenobarbital toxicity	Consider dose decreases of phenobarbital
Barbiturates, benzodiazepines, opioids	Additive CNS respiratory depression	Avoid concomitant use
Phenytoin	Increased or decreased phenytoin concentrations	Monitor phenytoin levels
Valproic acid	Increased risk of phenobarbital toxicity or decreased valproic acid efficacy	Monitor phenobarbital and valproic acid levels

Adverse Reactions: Phenobarbital

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Apnea, ataxia, confusion, dizziness, hypotension, hypoventilation, rash, somnolence, syncope	Barbiturate withdrawal, bradyarrhythmia, megaloblastic anemia

Efficacy Monitoring Parameters. Control of seizures, achieving adequate sleep; phenobarbital serum levels: therapeutic 10-40 mcg/mL; toxic >40 mcg/mL.

Toxicity Monitoring Parameters. SCr, LFTs, and CBC annually.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness, light-headedness, or somnolence. Advise patient against sudden discontinuation of drug. Do not drink alcohol or use other CNS depressant drugs while taking phenobarbital. Many drug interactions; check with pharmacist when starting new medications or OTC products.

Clinical Pearls. Efficacy for inducing and maintaining sleep begins to decline after ~2 wk; should not be used long term. Avoid use in children and elderly who are at higher risk of toxicity. Avoid abrupt withdrawal to decrease risk of seizures.

PHENTERMINE: Adipex-P, Various

Class: Centrally Acting Appetite Suppressant, C-IV

Dosage Forms. Oral Capsule: 15 mg, 30 mg, 37.5 mg; **Oral Tablet:** 37.5 mg; **Oral Dispersible Tablet:** 15 mg, 30 mg, 37.5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Simple obesity (BMI ≥30 kg/m^2 or >27 kg/m^2 with risk factors), short-term, adjunct treatment: 15-37.5 mg (capsules) or 37.5 mg (tablets) po daily either before breakfast or 1-2 h after breakfast; may titrate to response

Mutual Pharmaceutical generic 37.5 mg pictured

Off-Label Uses. None

MOA. Phentermine is a sympathomimetic amine with pharmacologic activity similar to amphetamines. Actions include CNS stimulation and elevation of BP. Weight loss is due to anorectic effect, primarily one of appetite suppression, but may also have other CNS or metabolic effects.

Drug Characteristics: Phentermine

Dose Adjustment Hepatic	Not required	**Absorption**	Not known
Dose Adjustment Renal	Not required	**Distribution**	Not known
Dialyzable	Unknown	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 80% with a half-life of 20 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to phentermine or other sympathomimetic amines, use in agitated states, cardiovascular disease, history of drug abuse, glaucoma, moderate to severe hypertension, hyperthyroidism	**Black Box Warnings**	None

Medication Safety Issues: Phentermine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Dispersible tablet	No	Phenytoin, Phentolamine	No

Drug Interactions: Phentermine

Typical Agents	Mechanism	Clinical Management
Fenfluramine, dexfenfluramine, TCAs	Unknown; combined use associated with primary pulmonary hypertension, valvular disorders, and death	Avoid concurrent use
MAOIs	Increases hypertensive effects of phentermine	Avoid phentermine within 14 d of MAOI discontinuation; do not use MAOIs within 5 wk of phentermine discontinuation

Adverse Reactions: Phentermine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Increased BP, palpitations, tachyarrhythmia, urticaria, constipation, diarrhea, xerostomia, dizziness, excitement, headache, insomnia, tremor, dysphoric mood, euphoria, restlessness	Heart valve disorder, psychotic disorder, primary pulmonary hypertension

Efficacy Monitoring Parameters. Weight loss.

Toxicity Monitoring Parameters. Signs and symptoms of heart valve disorders and primary pulmonary hypertension, ECG, BP.

Key Patient Counseling Points. Phentermine may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Clinical Pearls. Phentermine is indicated only as short-term monotherapy for the management of exogenous obesity. The safety and efficacy of combination therapy with phentermine and any other drug products for weight loss, including SSRIs, have not been established. Primary pulmonary hypertension and valvular heart disease have been reported to occur in patients receiving a combination of phentermine with fenfluramine or dexfenfluramine and should be avoided. Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Should be used in conjunction with a comprehensive weight management program.

PHENYTOIN: Dilantin, Various

Class: Hydantoin Anticonvulsant

Dosage Forms. Oral Capsule: 30 mg, 100 mg, 200 mg, 300 mg; **Oral Chewable Tablet**: 50 mg; **Oral Suspension:** 125 mg/5 mL

Taro generic 100 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Seizure, generalized tonic-clonic, complex partial, or following neurosurgery, treatment, and prophylaxis: Adults, 100 mg po tid, may titrate to 200 mg po tid; Children, 5 mg/kg/d po divided into 2-3 doses, may titrate to 300 mg/d

Off-Label Uses. None

MOA. Phenytoin is a hydantoin that suppresses the spread of seizure activity mainly by inhibiting synaptic post-tetanic potentiation and blocking the propagation of electric discharge. Phenytoin might decrease sodium transport and block calcium channels at the cellular level to produce these actions.

Drug Characteristics: Phenytoin

Dose Adjustment Hepatic	Monitor and consider dose adjustments	**Absorption**	F = 70-100%, food increases absorption
Dose Adjustment Renal	Monitor and consider dose adjustments	**Distribution**	Vd = 0.75 L/kg; 88-93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic, CYP2C19 and CYP2C9 substrate; strong inducer of CYP2B6, 2C19, 2C8, 2C9, and 3A4/5
Pregnancy Category	D	**Elimination**	Fecal elimination with a half-life of 7-42 h
Lactation	Compatible	**Pharmacogenetics**	Patient with HLA-B*1502 at increased risk of Stevens-Johnson syndrome
Contraindications	Hypersensitivity to phenytoin, sinus bradycardia, AV block	**Black Box Warnings**	Hypotension and arrhythmias with IV administration

Medication Safety Issues: Phenytoin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	ER capsules	Yes	PHENobarbital, Dilaudid, diltiazem	No

Drug Interactions: Phenytoin

Typical Agents	Mechanism	Clinical Management
CYP2C19, CYP2C9 inducers	Increased phenytoin metabolism reduces phenytoin effectiveness	Consider dose increases of phenytoin
CYP2C19, CYP2C9 inhibitors	Decreased phenytoin metabolism increases risk of phenytoin toxicity	Consider dose decreases of phenytoin
Substrates of CYP2B6, 2C19, 2C8, 2C9 and 3A4/5	Metabolism of substrates increased, reducing effectiveness of substrates	Consider increasing dose of substrate if necessary
Acetaminophen	Decreased acetaminophen efficacy and increased risk of hepatotoxicity	Avoid large and/or chronic acetaminophen doses; monitor for hepatotoxicity.
Carbamazepine, valproic acid	Altered phenytoin carbamazepine or valproic acid concentrations	Monitor concentrations; adjust doses as necessary

Adverse Reactions: Phenytoin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Gingival hyperplasia	Ataxia, confusion, constipation, decreased coordination, dizziness, feeling nervous, headache, hypertrichosis, impaired cognition, insomnia, intentional tremor, nausea, nystagmus, osteomalacia, peripheral neuropathy, rash, slurred speech, spasmodic movement, vomiting	Hepatotoxicity, pancytopenia, systemic lupus erythematosus, Stevens-Johnson syndrome, suicidal behavior, withdrawal seizures

Efficacy Monitoring Parameters. Reduction in the frequency and severity of seizures; phenytoin serum level range 10-20 mcg/mL (obtain after at least 5-7 half-lives after treatment initiation or dosage change).

Toxicity Monitoring Parameters. Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior; monitor CBC and LFTs.

Key Patient Counseling Points. Do not crush extended-release capsules. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report signs/symptoms of pancytopenia, hepatotoxicity, systemic lupus erythematosus, or severe skin reaction. Do not drink alcohol while taking this drug. Many drug interactions; check with health-care provider when starting new medications or OTC products.

Clinical Pearls. Highly protein bound, so albumin levels should be taken into account when measuring phenytoin concentration; dose adjustment based on free phenytoin concentration. Injectable formulation available, but not for use IM (causes “purple glove syndrome” related to tissue necrosis). Medication guide required at dispensing.

PIOGLITAZONE: Actos, Various

Class: Thiazolidinedione Antidiabetic

Dosage Forms. Oral Tablet: 15 mg, 30 mg, 45 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 2: 15-30 mg po daily; may titrate to *max* of 45 mg po daily as monotherapy, or in combination with sulfonylurea or metformin

Off-Label Uses. None

MOA. Pioglitazone is a thiazolidinedione antihyperglycemic and a potent peroxisome proliferator-activated receptor-γ (PPAR-γ) agonist used to improve insulin sensitivity in patients with type 2 diabetes. Insulin-dependent glucose disposal in skeletal muscle is improved and hepatic glucose production is decreased; both actions contribute to pioglitazone's glucose-lowering effects.

Takeda 30 mg pictured

Drug Characteristics: Pioglitazone

Dose Adjustment Hepatic	Avoid if LFTs elevated	**Absorption**	F = 50%, food delays but does not reduce absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.63 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2C8 substrate; moderate inhibitor of CYP2C8
Pregnancy Category	C	**Elimination**	Renal elimination is 15-30% with a half-life of 16-24 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to pioglitazone, NYHA III/IV heart failure	**Black Box Warnings**	Heart failure risk

Medication Safety Issues: Pioglitazone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Actidose, Actonel	No

Drug Interactions: Pioglitazone

Typical Agents	Mechanism	Clinical Management
CYP2C8 inducers	Increased pioglitazone metabolism reduces pioglitazone effectiveness	Consider dose increases of pioglitazone
CYP2C8 inhibitors	Decreased pioglitazone metabolism increases risk of pioglitazone toxicity	Consider dose decreases of pioglitazone
Substrates of CYP2C8	Metabolism of substrates decreased, increasing risk of toxicity	Monitor for toxicity and consider decreasing dose of substrate if necessary
Corticosteroids	May diminish or increase hypoglycemic effect of pioglitazone	Monitor and consider pioglitazone dose adjustment if chronic steroid use
NSAIDs, SSRIs	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Monitor blood glucose and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Monitor blood glucose and consider dose adjustments

Adverse Reactions: Pioglitazone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, weight gain	Myalgia, bone fractures, sinusitis, headache	Heart failure, anemia, hepatotoxicity, diabetic macular edema, hypoglycemia when used in combination with insulin or sulfonylureas

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7% (goal HbA_{1c} may be 6.5-8% based on patient-specific characteristics).

Toxicity Monitoring Parameters. Weight for assessment of edema, Hgb, LFTs; symptoms of hypoglycemia include, nausea, sweating, and loss of consciousness; seek care for bone pain, yellowing of skin or eyes, eye pain, or shortness of breath; eye exams.

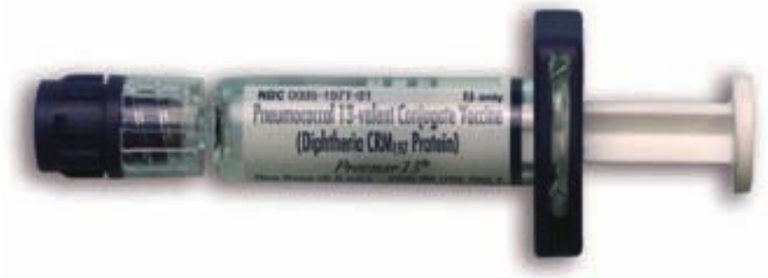
Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times per d). May take without regard to food. May require several weeks for max effect.

Clinical Pearls. Pioglitazone causes edema, which may exacerbate underlying heart failure; contraindicated with NYHA III/IV heart failure. Stimulates ovulation. Premenopausal anovulatory individuals may resume ovulation. Increased risk of pregnancy in premenopausal female diabetics; use effective birth control. Not for use in children. Medication guide required at dispensing.

PNEUMOCOCCAL VACCINE: Prevnar13, Pneumovax23

Class: Vaccine, Inactivated, Bacterial

Dosage Forms. **Suspension for Intramuscular Injection:** 0.5 mL (13 valent conjugate vaccine, PCV13, Prevnar13); **Solution for Intramuscular or Subcutaneous Injection:** 0.5 mL (23 valent polysaccharide vaccine, PPSV23, Pneumovax23)



Wyeth pictured

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of invasive pneumococcal disease: Adults ≥50 y of age, single dose IM once (either product); Children, single dose at 2, 4, 6, and 12-15 mo of age as primary series (conjugate product), multiple approved schedules for "catching up" in children who do not start their vaccine series on time

Off-Label Uses.

1. Prevention of invasive pneumococcal disease, immunosuppressed individuals ≥6 y of age: If vaccine naive, single-dose PCV13 IM once, followed by single dose PPSV23 IM once in 8 wk; if previously vaccinated with PPSV23, single-dose PCV13 IM at least 12 mo after last PPSV23
2. Prevention of invasive pneumococcal disease, individuals ≥65 y of age: If vaccine naive, single-dose PCV13 IM once, followed by single dose PPSV23 IM once in 6-12 mo; if previously vaccinated with PPSV23, single-dose PCV13 IM at least 12 mo after last PPSV23
3. Prevention of invasive pneumococcal disease in individuals at high risk for invasive pneumococcal disease, including asplenia, chronic heart disease, chronic lung disease, diabetes, cerebrospinal fluid leak, cochlear implant, alcoholism, chronic liver disease (including asthma if ≥19 y of age), cigarette smoker ≥19 y of age, hemoglobinopathy, immunocompromised (congenital or acquired, HIV infection, leukemia, lymphoma, generalized malignancy, iatrogenic immunosuppression, solid-organ transplant, multiple myeloma): single-dose PPSV23 IM once
4. Prevention of invasive pneumococcal disease in individuals at high risk for invasive pneumococcal disease, including asplenia, hemoglobinopathy, immunocompromised: Single dose PPSV23 IM once and repeat single dose IM once.

Merck pictured

Drug Characteristics: Pneumococcal Vaccine

Pregnancy Category	PCV13, B PPSV23, C	**ADME**	Not known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to pneumococcal vaccine or a component of the vaccine	**Black Box Warnings**	None

Medication Safety Issues: Pneumococcal Vaccine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Prevnar13, Pneumovax23	No

Drug Interactions: Pneumococcal Vaccine

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression reduces vaccine efficacy	Delay vaccination until corticosteroid therapy has been discontinued, if possible
Immunosuppressing agents	Diminished immune response to vaccine due to immunosuppression	Delay pneumococcal vaccine administration until immunosuppressive therapy has been discontinued, if possible
Herpes zoster vaccine	Immunologic interference	Concomitant administration with PPSV23 lowers antibody concentrations to zoster vaccine; clinical consequences are unknown and no change in efficacy observed if administered simultaneously; separate vaccines by 4 wk if follow-up assured

Adverse Reactions: Pneumococcal Vaccine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Rash, decreased appetite, arthralgia, myalgia, decreased sleep, somnolence, headache, asthenia	Diarrhea, vomiting, fever	Thrombocytopenia, anaphylaxis

Efficacy Monitoring Parameters. Prevention of invasive pneumococcal disease, including bacterial meningitis.

Toxicity Monitoring Parameters. Monitor for syncope, fever after administration.

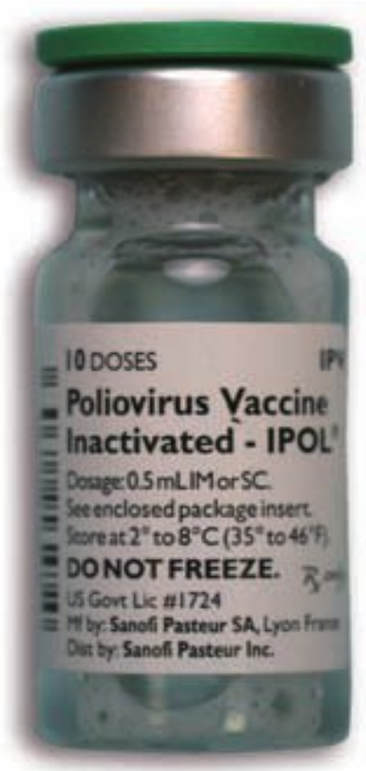
Key Patient Counseling Points. May administer antipyretics to reduce fever after vaccine administration.

Clinical Pearls. PCV13 used for routine immunization of infants and young children, for immunosuppressed individuals ≥6 y of age and those ≥65 y of age. PPSV23 should not be used in children <2 y of age. PPSV23 used for individuals with chronic diseases, including immunosuppressive diseases.

POLIOVIRUS VACCINE, INACTIVATED: Ipol

Class: Vaccine, Inactivated, Viral

Dosage Forms. Solution for Intramuscular or Subcutaneous Injection: 0.5 mL; also available in combination with other pediatric vaccines



Sanofi Pasteur pictured

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of poliomyelitis: Children, one 0.5-mL dose IM or sq at 2, 4, and 6-18 mo of age, and a booster at 4-6 y of age as primary series

Off-Label Uses.

1. Prevention of poliomyelitis, in adults previously vaccinated but who are at risk for polio exposure: One 0.5-mL dose IM or sq
2. Prevention of poliomyelitis, in adults previously incompletely vaccinated but who are at risk for polio exposure: One 0.5-mL dose IM or sq
3. Prevention of poliomyelitis, in adults previously unvaccinated but who are at risk for polio exposure: Two 0.5-mL doses IM or sq at 1-2 mo intervals followed by a 3rd dose 6-12 mo later

Drug Characteristics: Poliovirus Vaccine, Inactivated

Pregnancy Category	C	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to Hib vaccine or a component of the vaccine (2-phenoxyethanol, calf serum, formaldehyde, neomycin, polymixin, streptomycin)	**Black Box Warnings**	None

Medication Safety Issues: Poliovirus Vaccine, Inactivated

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	PPD	No

Drug Interactions: Poliovirus Vaccine, Inactivated

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression reduces vaccine efficacy	Delay vaccination until corticosteroid therapy has been discontinued, if possible
Immunosuppressing agents	Diminished immune response to vaccine due to immunosuppression	Delay vaccination until immunosuppressive therapy has been discontinued, if possible

Adverse Reactions: Poliovirus Vaccine, Inactivated

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness, loss of appetite, fatigue, irritability	Vomiting, fever	Anaphylaxis, febrile seizure, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of poliomyelitis.

Toxicity Monitoring Parameters. Monitor for syncope, fever after administration.

Key Patient Counseling Points. Return to provider for each dose in the series.

Clinical Pearls. Adults, even those without evidence of previous immunization, rarely need poliovirus vaccine. A single dose is needed only if exposure likely, such as travel to an endemic area (eg, Pakistan, Nigeria). The United States has been polio-free since 1979.

POLYETHYLENE GLYCOL: Golytely, Various

Class: Hyperosmotic Laxative

Dosage Forms. Powder for Oral Solution: 119-420 g

Common FDA Label Indication, Dosing, and Titration.

1. Colonoscopy or barium enema preparation: Adults, 17 g of powder dissolved in 240 mL of reconstituted solution po q10min until diarrhea is clear or 4 L are consumed or 20-30 mL/min via nasogastric tube until rectal effluent is clear or 4 L are administered
2. Constipation: Adults, 17g of powder dissolved in 240 mL of reconstituted solution once daily; Children, 0.5-1.5 g/kg po daily

Off-Label Uses.

1. Whole bowel irrigation after toxic ingestions, 240 mL of reconstituted solution q10min until diarrhea is clear or 4 L are consumed or 20-30 mL/min via nasogastric tube until rectal effluent is clear or 4 L are administered

MOA. Polyethylene glycol (PEG) electrolyte lavage solution is a hyperosmotic solution that includes various electrolytes (sodium sulfate, sodium bicarbonate, sodium chloride, potassium chloride).

Kremer Urban generic pictured

Drug Characteristics: Polyethylene Glycol

Dose Adjustment Hepatic	Not required	**Absorption**	Not absorbed
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Bowel perforation, gastric retention, GI obstruction, ileus, toxic colitis	**Black Box Warnings**	None

Medication Safety Issues: Polyethylene Glycol

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
C G	GoLYTELY, NuLYTRLY	No	No	NuLYTELY	No

Drug Interactions: Polyethylene Glycol

Typical Agents	Mechanism	Clinical Management
Potassium supplements	Additive hyperkalemia	Monitor serum potassium and SCr
Potassium-sparing diuretics	Additive hyperkalemia	Monitor serum potassium and SCr
ACE-Is	Additive hyperkalemia	Monitor serum potassium and SCr

Adverse Reactions: Polyethylene Glycol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Anal irritation, bloating symptom, epigastric fullness, nausea, stomach cramps, vomiting	Urticaria	Anaphylaxis, dehydration, seizures

Efficacy Monitoring Parameters. Bowel movements should begin within 60 min of initiating administration and dosing should continue until rectal effluent is clear if utilized as bowel preparation for imaging study.

Toxicity Monitoring Parameters. Seek medical attention if urticaria, rhinorrhea, or dermatitis occurs.

Key Patient Counseling Points. This preparation may cause nausea, anal irritation, or vomiting. If severe bloating, abdominal distension, or abdominal pain occurs, patient should slow the consumption of solution, and once symptoms have resolved, the patient may resume administration. If utilized as bowel preparation for imaging study, advise patient to avoid solid foods for 3-4 h before beginning this treatment.

Clinical Pearls. Encourage patients to drink each portion rapidly, as this method is preferred over drinking small amounts continuously. The solution tastes better chilled, but ice should not be added to the solution. Since oral medications are flushed from their system by this treatment and may not be absorbed, patients should receive guidance from the prescriber of PEG solution regarding whether and when to take oral doses of other medications. Risk of drug interactions resulting in hyperkalemia offset by diarrheal loss of potassium, clinical relevance uncertain.

POTASSIUM CHLORIDE: Klor-con, Various

Upsher-Smith pictured

Class: Electrolyte, Potassium

Dosage Forms. Oral Capsule, Extended Release: 8 mEq, 10 mEq; **Powder for Oral Solution:** 20 mEq, 25 mEq; **Oral Solution:** 20 mEq/15 mL; **Oral Tablet, Extended Release:** 8 mEq, 10 mEq, 15 mEq, 20 mEq

Common FDA Label Indication, Dosing, and Titration.

1. Hypokalemia: Adults, 20-100 mEq/d po divided 1-5 times daily after meals; Children, 3-8 mEq/d po divided 1-5 times daily after meals
2. Hypokalemia, prophylaxis: 20 mEq/d po daily

Off-Label Uses. None

MOA. Potassium is an electrolyte required for maintenance of the excitatory properties of neuromuscular tissues, and the resting membrane potential of cells is related to potassium concentrations, varying directly with the ratio of intracellular to extracellular potassium level.

Drug Characteristics: Potassium Chloride

Dose Adjustment Hepatic	Not required	**Absorption**	Well absorbed
Dose Adjustment Renal	Contraindicated	**Distribution**	98% of total body potassium is located intracellularly
Dialyzable	Yes	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 85-95%
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to potassium, acute renal failure, structural, pathological, or pharmacologic cause delay in tablet passage through the GI tract, hyperkalemia, Addison disease, acute dehydration	**Black Box Warnings**	None

Medication Safety Issues: Potassium Chloride

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
10, M10, M20, K	No	Do not crush extended-release products	Yes (IV)	HCl, Macrobid, Micronase	No

Drug Interactions: Potassium Chloride

Typical Agents	Mechanism	Clinical Management
Anticholinergics	Decreased GI motility and increased risk of erosions caused by potassium	Contraindicated
Potassium-sparing diuretics	Increased risk of hyperkalemia	Monitor potassium levels and consider alternative therapies
ACE-Is, ARBs	ACE-Is and ARBs may lower aldosterone levels, which may result in potassium retention	Monitor potassium levels

Adverse Reactions: Potassium Chloride

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nausea, indigestion, flatulence	Vomiting	ECG changes with hypokalemia or hyperkalemia, esophagitis

Efficacy Monitoring Parameters. Monitor serum potassium and adjust dose to maintain serum potassium in the normal range 3.5-5 mEq/L.

Toxicity Monitoring Parameters. SCr, ECG if hypokalemic or hyperkalemic.

Key Patient Counseling Points. Take with food. Take the powder, granule, or oral liquid only after mixing in 4 oz of water or juice. Crush or break only specifically designed extended-release formulations. Capsules may be opened, sprinkled on apple sauce, and ingested immediately.

Clinical Pearls. The total potassium content in a 70-kg male is approximately 3500 mEq. Some drugs (insulin, β-agonists) decrease potassium levels by causing an intracellular shift of potassium. If replacement does not normalize potassium level, check magnesium levels and calcium levels and replace as necessary.

POTASSIUM IODIDE: SSKI, ThyroShield, Various

Class: Antithyroid Agent

Dosage Forms. Oral Solution: 65 mg/mL (SSKI), 1 g/mL (ThyroShield)

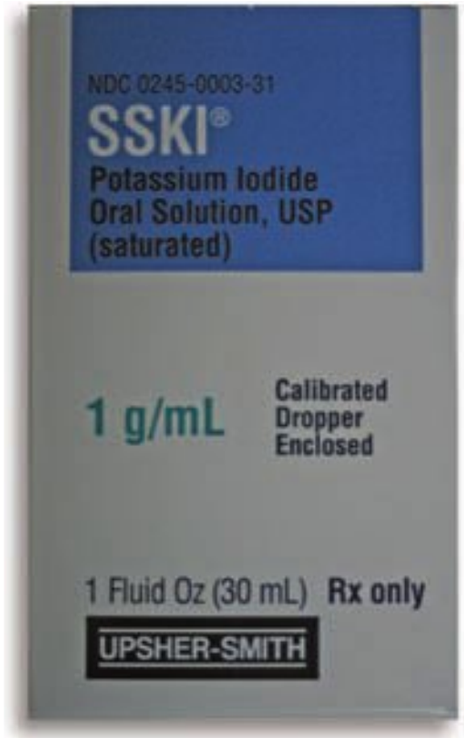
Common FDA Label Indication, Dosing, and Titration.

1. Prevention of thyroid dysfunction due to radiation exposure: Children, birth to 1 mo of age, 16.25 mg po daily; Children 1 mo to 3 y of age, 32.5 mg po daily; Children 3-12 y of age, 65 mg po daily; Children >12 y of age but <150 lb, 65 mg po daily; Children >12 y of age and ≥150 lb and Adults, 130 mg po daily

Off-Label Uses.

1. Induction or involution of thyroid: 60-250 mg po tid × 10 d preoperatively to reduce vascularity of the gland prior to thyroidectomy
2. Graves disease (short-term reduction in thyroid hormone production prior to ablation or surgery): 50 mg po q8h

MOA. Iodine is needed for the production of thyroid hormones. In patients with disorders causing hyperthyroidism, iodide is administered to inhibit the release of thyroid hormones via direct effect on the thyroid gland and inhibits synthesis of thyroid hormones. Also attenuates effects of TSH mediated via cAMPb and decreases vascularity of thyroid gland. When administered before or promptly after radioactive iodine exposure, potassium iodide blocks or reduces accumulation of radioactive iodine in the thyroid gland.



Upsher-Smith 1 g/mL solution pictured

Drug Characteristics: Potassium Iodide

Dose Adjustment Hepatic	Not required	**Absorption**	Readily absorbed
Dose Adjustment Renal	Not required	**Distribution**	Iodide concentrates in the thyroid gland, salivary glands, gastric mucosa, choroid plexus, placenta, and mammary glands
Dialyzable	Yes	**Metabolism**	Taken up by the thyroid; not metabolized
Pregnancy Category	D	**Elimination**	Renal elimination is 85-90%
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to potassium iodide	**Black Box Warnings**	None

Medication Safety Issues: Potassium Iodide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Potassium iodine	No

Drug Interactions: Potassium Iodide

Typical Agents	Mechanism	Clinical Management
Warfarin	Hyperthyroid patients metabolize clotting factors more quickly than normal. By decreasing thyroid hormone production, potassium iodide may alter metabolism of clotting factors and affect the INR	Monitor INR carefully and adjust warfarin dose as required

Adverse Reactions: Potassium Iodide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Stomach upset, diarrhea, nausea, vomiting, stomach pain	Rash, salivary gland swelling or tenderness	Goiter, hypothyroidism, thyroid adenoma, immune hypersensitivity reaction

Efficacy Monitoring Parameters. Thyroid function tests.

Toxicity Monitoring Parameters. Serum potassium, SCr, BUN, signs/symptoms of goiter, hypothyroidism, thyroid adenoma, allergic reaction, hyperkalemia.

Key Patient Counseling Points. To minimize GI irritation, administer with food. Take with 4 oz of water. Other liquids can be used; dilution in chocolate milk can mask the taste. During a radiation emergency, understand the nature of the radiation hazard and the potential benefits and adverse effects of potassium iodide. Administer potassium iodide only as directed by public health authorities. Adhere to other emergency measures recommended by public health authorities.

Clinical Pearls. Potassium iodide has been used in the past as an expectorant and cough suppressant, which is not appropriate given the risk of adverse effects. Potassium iodide crosses into breast milk, but most guidelines consider it compatible with breast-feeding.

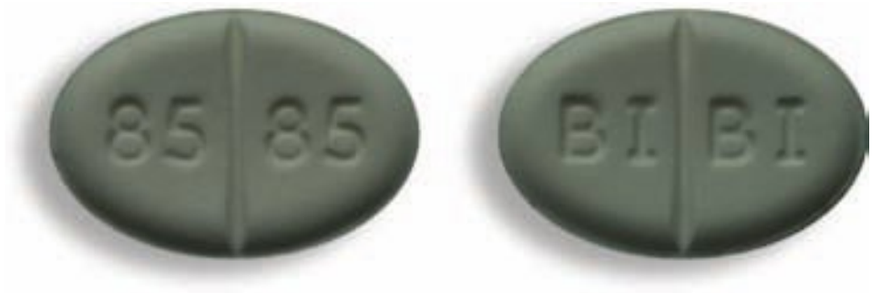
PRAMIPEXOLE: Mirapex, Mirapex ER

Class: Dopamine Agonist, Anti-Parkinson

Dosage Forms. Oral Tablet: 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg; **Oral Tablet, Extended Release):** 0.375 mg, 0.75 mg, 1.5 mg, 2.25, 3 mg, 3.75 mg, 4.5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Parkinson disease: Immediate release, 0.125 mg po tid, may titrate to 0.5-1.5 mg po tid; extended release, 0.375 mg po daily, may titrate to 4.5 mg po daily
2. Restless legs syndrome: 0.125 mg po daily taken 2-3 h prior to bedtime, may titrate to 0.5 mg po daily



Boehringer Ingelheim 0.5 mg pictured

Off-Label Uses. None

MOA. Pramipexole is a nonergot-derived dopamine subtype selective agonist that exerts activity in the CNS at D_2 and D_3 receptors but has no activity at the D_1 receptor. D_2 receptors are thought to play an important role in improving the akinesia, bradykinesia, rigidity, and gait disturbances of Parkinson disease.

Drug Characteristics: Pramipexole

Dose Adjustment Hepatic	No adjustment needed	**Absorption**	F = 90%, food reduces Tmax
Dose Adjustment Renal	Immediate release: CrCl 35-50 mL/min, 0.125 mg po bid, to *max* of 1.5 mg po bid; CrCl 15-34 mL/min, 0.125 mg po daily, to *max* of 1.5 mg po daily, CrCl <15 mL/min: avoid; Extended release: CrCl 30-50 mL/min, 0.375 mg po qod, to *max* of 2.25 mg po daily; CrCl <30 mL/min: avoid	**Distribution**	Vd = 500 L; 15% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 90% with a half-life of 8-12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to pramipexole	**Black Box Warnings**	None

Medication Safety Issues: Pramipexole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ER	No	Extended-release tablets	No	MiraLax	No

Drug Interactions: Pramipexole

Typical Agents	Mechanism	Clinical Management
Cimetidine	Increased pramipexole concentrations	Choose an alternative acid-reducing agent
Antipsychotics	May reduce the effectiveness of antipsychotic or dopamine agonists	Avoid, or monitor effect of both agents and increase dose if necessary

Adverse Reactions: Pramipexole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Asthenia, dream disorder, dyskinesia, extrapyramidal movements, nausea, somnolence	Amnesia, confusion, compulsive behavior, constipation, diarrhea, dizziness, fatigue, hallucinations, headache, insomnia, orthostatic hypotension, peripheral edema, xerostomia	Blackouts, heart failure, impulsive behavior, melanoma

Efficacy Monitoring Parameters. Improvement in Parkinson symptoms or restless legs syndrome.

Toxicity Monitoring Parameters. Hypotension, drowsiness, hallucinations, or behavior changes; melanoma screening.

Key Patient Counseling Points. Take with food if nausea occurs. Avoid activities requiring mental alertness or coordination until drug effects are realized. Rise slowly from a sitting/lying down position. Report new or increased gambling urges, sexual urges, compulsive eating or buying, as well as new-onset or worsening dyskinesia. Do not discontinue abruptly, as this may cause emergent hyperpyrexia and confusion. Do not drink alcohol, and avoid concomitant use of other CNS depressants.

Clinical Pearls. Safety and efficacy in children not established. May switch patient from immediate-release to extended-release tablets overnight at same daily dose.

PRASUGREL: Effient

Class: Antiplatelet Agent

Dosage Forms. Oral Tablet: 5 mg, 10 mg

Lilly 10 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of thromboembolism after percutaneous coronary intervention: 60 mg po once, then 10 mg po daily, in combination with aspirin 75-325 mg po daily

Off-Label Uses.

1. Prevention of thromboembolism in acute coronary syndrome: 30 mg po once, then 10 mg po daily, in combination with aspirin ≤100 mg po daily

MOA. Prasugrel is an inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the $P2Y_{12}$ class of ADP receptors on platelets.

Drug Characteristics: Prasugrel

Dose Adjustment Hepatic	Not required for mild or moderate impairment; risk in severe impairment not known	**Absorption**	F = 79%, food delays rate but not extent of absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 44-68 L; 98% albumin bound
Dialyzable	Not known	**Metabolism**	Rapid hepatic metabolism to active metabolite, which is further metabolized in the liver to an active metabolite
Pregnancy Category	B	**Elimination**	Renal elimination is 68-70% with a half-life of 7-8 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Active bleeding, history of transient ischemic attack or stroke	**Black Box Warnings**	Bleeding risk; not recommended in patients ≥75 y of age; CABG

Medication Safety Issues: Prasugrel

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Pravastatin	No

Drug Interactions: Prasugrel

Typical Agents	Mechanism	Clinical Management
SSRIs	Serotonin released from platelets is necessary for hemostasis; bleeding can result if antiplatelet agents are given with SSRIs	Monitor for bleeding
Antiplatelet agents, NSAIDs, and anticoagulants	Additive risk of bleeding	Avoid concurrent use or monitor carefully and adjust dose if necessary

Adverse Reactions: Prasugrel

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Hypertension, hyperlipidemia, backache, headache, epistaxis	Atrial fibrillation, colon cancer, major bleeding, TTP, angioedema

Efficacy Monitoring Parameters. Stent patency and prevention of clotting.

Toxicity Monitoring Parameters. Monitor for signs and symptoms of bleeding. Consider periodic hematocrit/hemoglobin, as well as platelet function testing.

Key Patient Counseling Points. May be given with or without food. Tablet may be crushed, but should not be split for purposes of dividing doses.

Clinical Pearls. After percutaneous coronary intervention, continue for 12 mo if stent is placed, and at least 15 mo if drug-eluting stent is placed. In patients weighing <60 kg, may consider dose of 5 mg po daily. May need to hold prior to surgical intervention; consult with cardiologist.

PRAVASTATIN: Pravachol, Various

Class: HMG-CoA Reductase Inhibitor

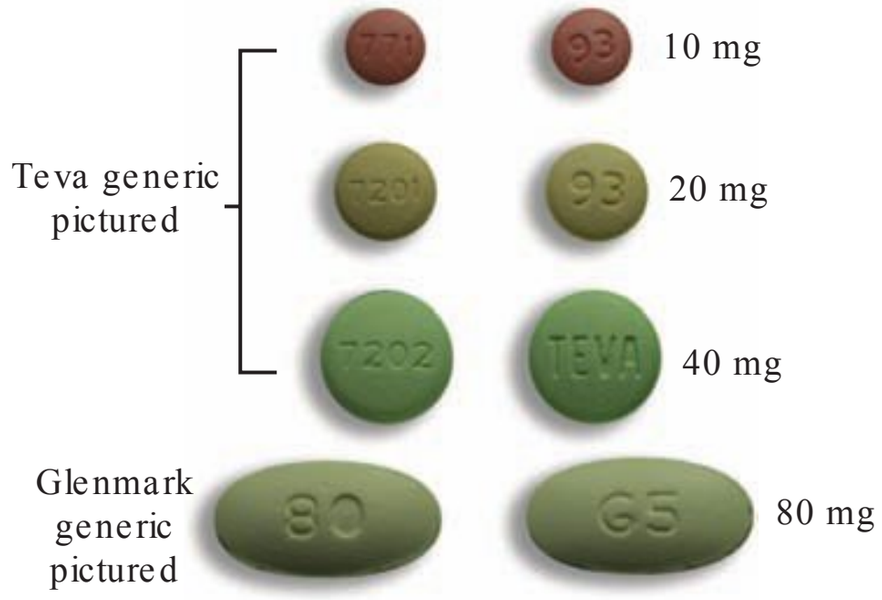
Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg, 80 mg

Common FDA Label Indication, Dosing, and Titration.

1. Cerebrovascular accident (prevention), coronary arteriosclerosis (primary or secondary prevention): 40 mg po daily
2. Familial hypercholesterolemia: Children 8-13 y of age, 20 mg po daily; Children 14-18 y of age, 40 mg po daily
3. Hyperlipidemia: Children (boys and postmenarchal girls) 10-17 y of age, 10 mg po daily, may titrate to 20 mg/d; Adults, 40 mg po daily, may titrate to 40-80 mg po daily

Off-Label Uses. None

MOA. HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol can decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.



Drug Characteristics: Pravastatin

Dose Adjustment Hepatic	Avoid use in patients with active liver disease or unexplained persistent elevated LFTs	**Absorption**	F = 17%, food has no effect on absorption
Dose Adjustment Renal	Initial dose 10 mg po daily	**Distribution**	Vd = 0.46 L/kg; 43-55% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic via hydroxylation
Pregnancy Category	X	**Elimination**	Renal elimination is 20% with a half-life of 2.6-3.2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Effective in lowering lipids in patients with the ApoE E2/E2 genotype and Fredrickson type III dysbetalipoproteinemia
Contraindications	Hypersensitivity to pravastatin, pregnancy or lactation	**Black Box Warnings**	None

Medication Safety Issues: Pravastatin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Prevacid, prasugrel	No

Drug Interactions: Pravastatin

Typical Agents	Mechanism	Clinical Management
Bile acid–binding resins	Binding by bile acid resins decrease efficacy of pravastatin	Give pravastatin 1 h before or 4 h after resin
Efavirenz, nelfinavir	Decreased pravastatin levels decreases efficacy of pravastatin	Monitor fasting lipid panels
Fibrates, niacin, cyclosporine	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use or monitor for myopathy and measure creatine kinase levels

Adverse Reactions: Pravastatin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Headache, heartburn, increased liver enzymes, influenza-like symptoms, musculoskeletal pain, myalgia, nausea, rash, vomiting	Rhabdomyolysis, tendon rupture

Efficacy Monitoring Parameters. Baseline fasting lipid panel (total cholesterol, LDL, HDL, and triglycerides), repeat 4-12 wk after initiation or dose adjustment.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs at baseline and if concern for hepatotoxicity; check serum creatine kinase in patients experiencing myopathy.

Key Patient Counseling Points. Take in the evening. Contraindicated in pregnancy. Avoid concurrent heavy alcohol use. Pravastatin does not take the place of diet and exercise to lower cholesterol levels.

Clinical Pearls. Repeat fasting lipid panel 4-12 wk following initiation or titration. Consider holding pravastatin 4-7 d before major surgery as patient is at higher risk for occurrence of rhabdomyolysis. May increase the risk of diabetes.

PREDNISOLONE ORAL: Orapred, Prelone, Various

Class: Adrenal Glucocorticosteroid

Dosage Forms. **Oral Tablet:** 5 mg; **Oral Dispersible Tablet:** 10 mg, 15 mg, 30 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL, 15 mg/5 mL 20 mg/5 mL; **Oral Syrup:** 15 mg/5 mL; **Oral Suspension:** 15 mg/5 mL

Common FDA Label Indication, Dosing, and Titration.

Dosing for indications listed below: Adults, 5-60 mg po daily; Children, 0.1-2 mg/kg/d; adjust dose according to patient response

1. Allergic states (eg, asthma, etc): 1-2 mg/kg/d divided 1-2 times daily, *max* of 60 mg/dose
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

Off-Label Uses.

1. Croup: 1 mg/kg po once

MGP generic 15 mg /5 mL solution pictured

MOA. Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids that cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

Drug Characteristics: Prednisolone Oral

Dose Adjustment Hepatic	Not required	**Absorption**	F = 85%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.5 L/kg; 70-90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Primarily renal elimination with a half-life of 2-4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to prednisolone or other glucocorticosteroids, administration of live vaccines, fungal infections	**Black Box Warnings**	None

Medication Safety Issues: Prednisolone Oral

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
DP, ODT, PRED, 20	PrednisoLONE	Dispersible tablet	No	PredniSONE	No

Drug Interactions: Prednisolone Oral

Typical Agents	Mechanism	Clinical Management
Antacids	Decreased absorption of corticosteroids	Separate administration by 2 h
CYP3A4/5 inhibitors	Decreased prednisolone metabolism increases risk of prednisolone toxicity	Monitor for toxicity and reduce prednisolone dose if necessary
CYP3A4/5 inducers	Increased prednisolone metabolism decreases prednisolone efficacy	Monitor for lack of efficacy and consider dose increase of prednisolone
Fluoroquinolones	Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly	Avoid concurrent use, or monitor carefully for tendon rupture
Phenytoin	Phenytoin increases prednisolone metabolism; prednisolone can increase or decrease phenytoin metabolism	Monitor prednisolone efficacy and phenytoin concentrations
Warfarin	Steroids can increase or decrease INR in patients taking warfarin	Monitor INR carefully

Adverse Reactions: Prednisolone Oral

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
GI upset	Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia	Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection

Efficacy Monitoring Parameters. Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

Toxicity Monitoring Parameters. Hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection. Mood changes may also occur; frequency and severity of adverse effects are dependent on the length of treatment and dose.

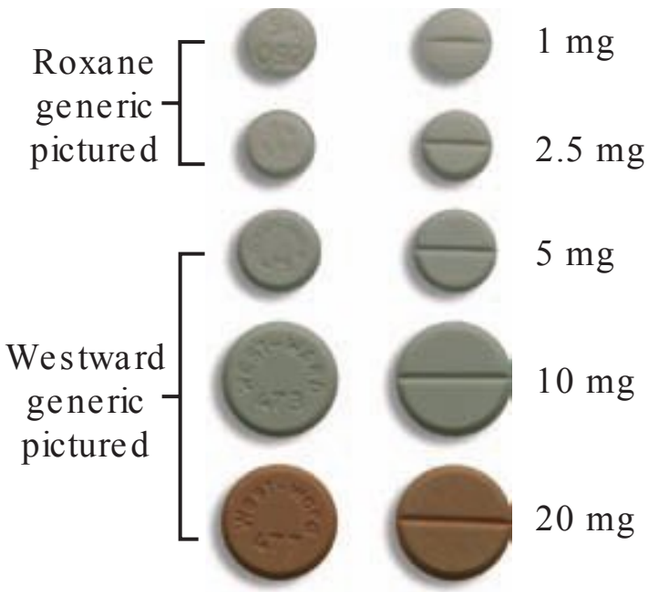
Key Patient Counseling Points. Take with food or milk to prevent GI upset. Take in the morning to help prevent insomnia. For high-dose or longer term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

Clinical Pearls. Available in a variety of dosage forms and concentrations, including ophthalmic preparations. Use lowest effective dose and discontinue as soon as possible to avoid serious long-term adverse effects. Some formulations taste worse than others; chocolate milk may mask taste best; oral disintegrating tablets are an expensive alternative. Taper required after chronic use (courses >14 d). 1 mg prednisolone is typically equivalent to 1 mg prednisone.

PREDNISONE: Deltasone, Various

Class: Adrenal Corticosteroid

Dosage Forms. Oral Tablet: 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg; **Oral Tablet, Delayed Release:** 1 mg, 2 mg, 5 mg; **Oral Solution:** 5 mg/1 mL; 5 mg/5 mL



Common FDA Label Indication, Dosing, and Titration.

Dosing for indications listed below: Adults and Children, 5-60 mg po daily; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

Off-Label Uses.

1. Graft-versus-host disease: 60 mg/m^2 po daily

MOA. Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids that cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

Drug Characteristics: Prednisone

Dose Adjustment Hepatic	Not required	**Absorption**	F = 92%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.4-1 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Primarily renal elimination with a half-life of 2.6-3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to prednisone or other glucocorticosteroids, administration of live vaccines, fungal infections	**Black Box Warnings**	None

Medication Safety Issues: Prednisone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Intensol	PredniSONE	Delayed-release formulation	No	prednisoLONE	No

Drug Interactions: Prednisone

Typical Agents	Mechanism	Clinical Management
Antacids	Decreased absorption of corticosteroids	Separate administration by 2 h
CYP3A4/5 inhibitors	Decreased prednisone metabolism increases risk of prednisone toxicity	Monitor for toxicity and reduce prednisone dose if necessary
CYP3A4/5 inducers	Increased prednisone metabolism decreases prednisone efficacy	Monitor for lack of efficacy and consider dose increase of prednisolone
Fluoroquinolones	Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly	Avoid concurrent use, or monitor carefully for tendon rupture
Phenytoin	Phenytoin increases prednisone metabolism; prednisone can increase or decrease phenytoin metabolism	Monitor prednisone efficacy and phenytoin concentrations
Warfarin	Steroids can increase or decrease INR in patients taking warfarin	Monitor INR carefully

Adverse Reactions: Prednisone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
GI upset	Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia	Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection

Efficacy Monitoring Parameters. Improvement or resolution of clinical signs and symptoms.

Toxicity Monitoring Parameters. Monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

Key Patient Counseling Points. Take with food or milk to prevent GI upset. Take in the morning to help prevent insomnia. For high-dose or longer term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

Clinical Pearls. See National Heart, Lung, and Blood Institute guidelines for dosing of prednisone for moderate to severe asthma exacerbation; after chronic use (>2 wk), dose tapering required prior to discontinuation of therapy.

PREGABALIN: Lyrica

Class: Analgesic, Anticonvulsant. C-V

Dosage Forms. Oral Capsule: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg; **Oral Solution:** 20 mg/mL

Pfizer pictured

Common FDA Label Indication, Dosing, and Titration.

1. Neuropathic pain, diabetes associated or spinal cord injury associated: 50-100 mg po tid
2. Fibromyalgia: 75-150 mg po bid; may titrate to *max* 225 mg bid
3. Partial seizure, adjunct: 25-75 mg po bid; may titrate to *max* 600 mg/d in 2-3 divided doses
4. Postherpetic neuralgia: Initial, 75 mg po bid; may titrate to 300 mg/d; maintenance 75-150 mg bid or 50-100 mg tid; may titrate to *max* 600 mg/d

Off-Label Uses. None

MOA. Pregabalin is a GABA analogue that strongly binds to the α_2-delta site (a subunit of voltage-gated calcium channels) in CNS tissues. Binding to the α_2-delta subunit may be involved in pregabalin's effects on neuropathic pain and seizure control. Pregabalin reduces the calcium-dependent release of several neurotransmitters; however, the exact mechanism of action is unknown.

Drug Characteristics: Pregabalin

Dose Adjustment Hepatic	Not required	**Absorption**	F >90%, food has no effect on absorption
Dose Adjustment Renal	CrCl 30-60 mL/min, 75-300 mg/d; CrCl 15-30 mL/min, 25-150 mg/d; CrCl <15 mL/min, 25-75 mg/d	**Distribution**	Vd = 0.5 L/kg; no protein binding
Dialyzable	Yes	**Metabolism**	Negligible hepatic metabolism
Pregnancy Category	C	**Elimination**	Renal elimination is 90-99% with a half-life of 5-6.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to pregabalin	**Black Box Warnings**	None

Medication Safety Issues: Pregabalin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Lopressor, Hydrea	No

Drug Interactions: Pregabalin

Typical Agents	Mechanism	Clinical Management
CNS depressants	Additive CNS depression	Consider dose reduction of pregabalin or other agent

Adverse Reactions: Pregabalin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, somnolence, ataxia, headache, peripheral edema	Arthralgia, asthenia, blurred vision, confusion, constipation, diplopia, disturbance in thinking, euphoria, fatigue, incoordination, increased appetite, muscle spasm, tremor, vomiting, weight gain, xerostomia	Angioedema

Efficacy Monitoring Parameters. Reduction in seizure frequency, improvement in pain, reduced symptoms of fibromyalgia.

Toxicity Monitoring Parameters. Creatine kinase, emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior, symptoms of angioedema, during initial and chronic therapy.

Key Patient Counseling Points. Solution must be used within 45 d of first opening the bottle. Avoid activities requiring mental alertness or coordination until drug effects are realized. Avoid sudden discontinuation of drug due to risk of withdrawal, including increased seizure frequency. Avoid drinking alcohol.

Clinical Pearls. Safety and efficacy have not been established in children. Data suggest an increased risk of suicidal behavior or ideation may exist in patients receiving therapy with AEDs.

PRENATAL VITAMIN: Various

Class: Vitamin Supplement

Dosage Forms. Oral Tablet: Containing various combinations of vitamins and minerals, including folic acid and iron

Amneal generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Diet supplementation during pregnancy: 1 tablet po daily

Off-Label Uses. None

MOA. Provide vitamin and mineral supplementation throughout pregnancy and during the postnatal period for both the lactating and the nonlactating mother. It is also useful for improving nutritional status prior to conception.

Drug Characteristics: Prenatal Vitamin

Dose Adjustment Hepatic	Not required	**Absorption**	Unknown
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Unknown
Pregnancy Category	A	**Elimination**	Unknown
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to any component of vitamin and mineral supplement	**Black Box Warnings**	Iron toxicity

Medication Safety Issues: Prenatal Vitamin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Prenatal Vitamin. None known

Adverse Reactions: Prenatal Vitamin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea, vomiting, constipation	

Efficacy Monitoring Parameters. Improvement in nutritional status.

Toxicity Monitoring Parameters. Seek medical attention if severe GI distress occurs.

Key Patient Counseling Points. May contain iron, so important to keep out of the reach of children.

Clinical Pearls. Various prescription and OTC products are available. May take with food to avoid GI upset, but administration with milk will decrease extent of iron absorption.

PROCHLORPERAZINE: Compazine, Various

Class: Phenothiazine

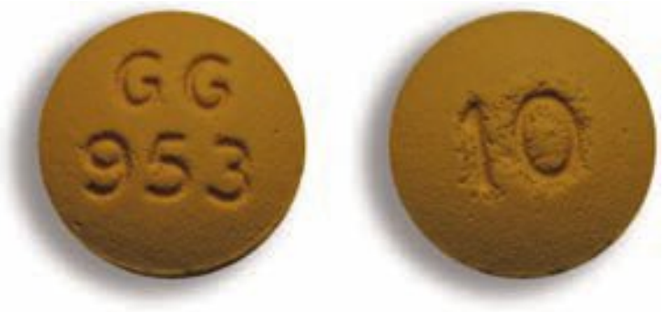
Dosage Forms. Oral Tablet: 5 mg, 10 mg; **Rectal Suppositories:** 25 mg

Common FDA Label Indication, Dosing, and Titration.

1. Nausea and vomiting: Adults, 5-10 mg po 3-4 times daily; daily dosages above 40 mg should be used only in resistant cases; Children ≥2 y of age and 20-29 lb, 2.5 mg po or pr daily-bid, *max* of 7.5 mg/d; Children 30-39 lb, 2.5 mg po or pr bid-tid, *max* 10 mg/d; Children 40-85 lb, 2.5-5 mg po or pr tid, *max* of 15 mg/d

Off-Label Uses. None

MOA. Prochlorperazine is dopamine (D_2) receptor antagonist that belongs to the phenothiazine class of antipsychotic agents.



Goldline 10 mg generic pictured

Drug Characteristics: Prochlorperazine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 12.5%, food has minimal effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 12.9-17 L/kg
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Half-life of 7-9 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to phenothiazines, bone marrow depression, children <20 lb or 2 y of age, comatose or greatly depressed states, severe hypotension	**Black Box Warnings**	Mortality in elderly with dementia

Medication Safety Issues: Prochlorperazine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	ChlorproMAZINE	No

Drug Interactions: Prochlorperazine

Typical Agents	Mechanism	Clinical Management
Agents that prolong the QT interval	Additive QT prolongation	Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids	Additive CNS depression	Monitor and consider dose adjustments
Dopamine agonists	Decreased effect of dopamine agonists	Avoid concurrent use
MAOIs	Additive respiratory depression, increased risk of serotonin syndrome	Contraindicated

Adverse Reactions: Prochlorperazine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Somnolence	Headache	Respiratory depression, hypotension, neuroleptic malignant syndrome, agranulocytosis, extrapyramidal symptoms (increased risk in children <5 y of age), seizures, QTc prolongation

Efficacy Monitoring Parameters. Resolution of nausea and vomiting.

Toxicity Monitoring Parameters. Excessive drowsiness, decreased breathing, seizures, unusual bruising or bleeding.

Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid concurrent use of other CNS depressants.

Clinical Pearls. Use caution in elderly; appear more sensitive to the effects. Prochlorperazine is FDA approved for schizophrenia, although seldom used. Atypical antipsychotics are generally more effective and less toxic. Injection contains benzyl alcohol, which can cause gasping syndrome in neonates; should be avoided.

PROGESTERONE: Prometrium, Various

Class: Progestin Hormone

Dosage Forms. **Oral Capsule:** 100 mg, 200 mg; **Vaginal Jelly:** 4%, 8%

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of estrogen-induced endometrial hyperplasia: 200 mg po daily hs × 12 sequential d per 28-d cycle while conjugated estrogens are administered
2. Secondary physiologic amenorrhea: 400 mg po daily hs × 10 d

Off-Label Uses. None

MOA. Progesterone transforms proliferative endometrium into secretory endometrium. Parenterally administered progesterone inhibits gonadotropin production, which in turn prevents follicular maturation and ovulation.

Solvay 100 mg pictured

Drug Characteristics: Progesterone

Dose Adjustment Hepatic	Mild, moderate, lower dose; severe, avoid	**Absorption**	F = 10-15%, food increases AUC
Dose Adjustment Renal	Not required	**Distribution**	90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 and CYP2C19 substrate
Pregnancy Category	B	**Elimination**	Renal elimination of metabolites, 50-60%, with half-life of 25 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Abnormal vaginal bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of DVT or PE, known or suspected pregnancy	**Black Box Warnings**	Cardiovascular disorders, breast cancer, dementia risk

Medication Safety Issues: Progesterone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Yes	No	No	No

Drug Interactions: Progesterone

Typical Agents	Mechanism	Clinical Management
CYP2C19, CYP3A4/5 inducers	Increased progesterone metabolism reduces progesterone effectiveness	Consider dose increases of progesterone
CYP2C19, CYP3A4/5 inhibitors	Decreased progesterone metabolism increases risk of progesterone toxicity	Consider dose decreases of progesterone
Warfarin	Progesterone may increase or decrease warfarin effectiveness; mechanism unknown	Monitor INR

Adverse Reactions: Progesterone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Weight change, headache, amenorrhea, breast tenderness, abdominal pain	Nausea, asthenia, feeling nervous, break-through bleeding	Thromboembolism (DVT, PE), thrombophlebitis, osteoporosis

Efficacy Monitoring Parameters. Resolution of clinical signs of abnormal bleeding or symptoms being managed with this product.

Toxicity Monitoring Parameters. Annual physical including BP monitoring and annual breast exam; diagnostic evaluation to rule out malignancy in event of persistent or recurring vaginal bleeding.

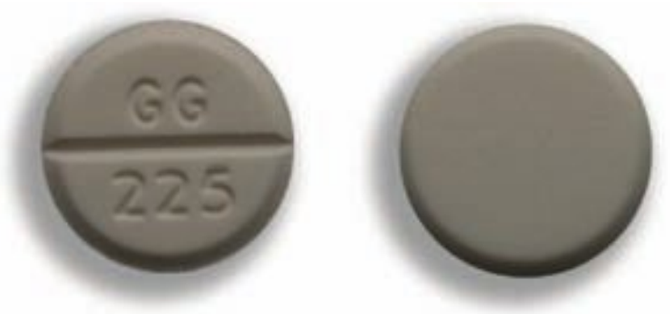
Key Patient Counseling Points. Advise patients that menstrual bleeding should occur 3-7 d after last dose. Patient should report if menstruation does not occur within 7 d after last dose.

Clinical Pearls. Injectable depot formulation of progesterone (medroxyprogesterone) is used for contraception (150 mg IM q3mo). Topical formulation is also available for other indications. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk of myocardial infarction, stroke, invasive breast cancer, PE, and DVT has been shown in postmenopausal women. Evidence regarding teratogenicity is conflicting; some studies show birth defects, and other studies show no effect.

PROMETHAZINE: Phenergan, Various

Class: Phenothiazine Antihistamine

Dosage Forms. Oral Syrup: 6.25 mg/5 mL; **Oral Tablet:** 12.5 mg, 25 mg, 50 mg; **Oral Solution:** 6.25 mg/5 mL; **Rectal Suppository:** 12.5 mg, 25 mg, 50 mg



Sandoz generic 25 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Motion sickness: Adults, 25 mg po or pr bid; Children ≥2 y of age, 12.5-25 mg po or pr bid
2. Allergy: Adults, 25 mg po or pr daily hs or 12.5 mg po or pr tid; Children ≥2 y of age, 25 mg po or pr daily hs or 6.25 mg po or pr tid
3. Nausea and vomiting: Adults, 25 mg po or pr q4-6h prn; Children ≥2 y of age, 12.5 mg po or pr q4-6h prn

Off-Label Uses. None

MOA. Promethazine hydrochloride is a phenothiazine derivative that competitively blocks histamine H_1 receptors without blocking the secretion of histamine. The drug has sedative, antimotion-sickness, antiemetic, and anticholinergic effects, but it has no dopaminergic action due to a structural difference with other phenothiazines.

Drug Characteristics: Promethazine

Dose Adjustment Hepatic	Not required, but use with caution	**Absorption**	Well absorbed with high first-pass metabolism; minimal effect of food absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 171 L; 93% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP2B6 and CYP2D6 substrate
Pregnancy Category	C	**Elimination**	Renal elimination of metabolites with a half-life of 9-16 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to promethazine, asthma, children <2 y, comatose state	**Black Box Warnings**	Children <2 y (fatal respiratory depression), tissue injury (IV)

Medication Safety Issues: Promethazine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes (IV only)	PredniSONE, chlorproMAZINE	Avoid. Highly anticholinergic

Drug Interactions: Promethazine

Typical Agents	Mechanism	Clinical Management
CYP2B6 inducers	Increased promethazine metabolism reduces promethazine effectiveness	Consider dose increases of promethazine
CYP2B6, CYP2D6 inhibitors	Decreased promethazine metabolism increases risk of promethazine toxicity	Consider dose decreases of promethazine
Anticholinergics	Additive anticholinergic effects	Avoid concurrent use
Agents that prolong the QT interval	Additive QT prolongation	Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids	Additive CNS depression	Monitor and consider dose adjustments
MAOIs	Additive respiratory depression, increased risk of serotonin syndrome	Contraindicated

Adverse Reactions: Promethazine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Somnolence, xerostomia	Constipation, nausea	Respiratory depression, hypotension, neuroleptic malignant syndrome, agranulocytosis, extrapyramidal symptoms, seizures, photosensitivity

Efficacy Monitoring Parameters. Relief of nausea or allergy symptoms.
Toxicity Monitoring Parameters. Mental status, vital signs.
Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.
Clinical Pearls. Use caution in elderly; appear more sensitive to the anticholinergic adverse effects.

PROPRANOLOL: Inderal, Inderal LA, Inderal XL, Various

Class: β-Adrenergic Blocker, Nonselective

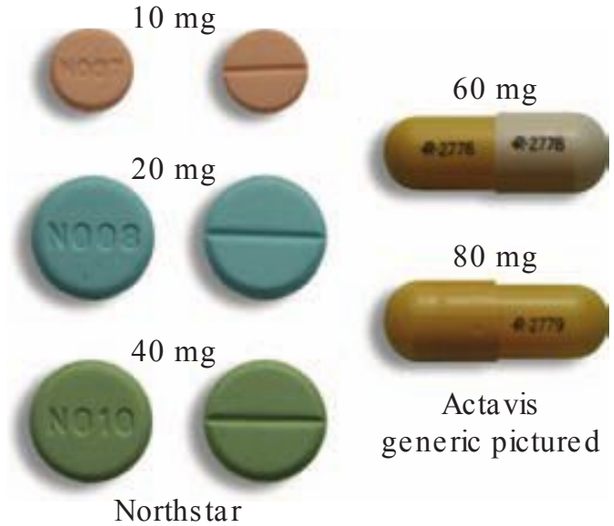
Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg, 60 mg, 80 mg; **Oral Capsule, Extended Release:** 60 mg, 80 mg, 120 mg, 160 mg; **Oral Solution:** 20 mg/5 mL, 40 mg/5 mL, 4.28 mg/mL

Common FDA Label Indication, Dosing, and Titration.

1. Angina pectoris, chronic: Immediate release, 80-320 mg po daily in 2-4 doses; extended release, 80-160 mg po daily
2. Cardiac dysrhythmia: Adults, 10-30 mg po tid-qid; Children, 2-6 mg/kg po in 3-4 doses, *max* 60 mg/d
3. Hypertension: Adults, immediate release, 40 mg po bid, may titrate to 240 mg po daily in 2-3 doses; Adults, extended release, 80 mg po daily, may titrate to 160 mg po daily; Children, immediate release, 0.5-1 mg/kg po daily in 3-4 doses, may titrate to 16 mg/kg/d
4. Migraine, prophylaxis: Immediate release, 80 mg po daily in divided doses, may titrate to 240 mg po daily; extended release, 80 mg po daily; may titrate to 240 mg po daily

Off-Label Uses.

1. Anxiety: 10 mg po 1 h prior to event



Northstar Rx generic pictured

Actavis generic pictured

MOA. Propranolol is a nonselective β-adrenergic blocker (class II antiarrhythmic) that competitively blocks β_1 and β_2 receptors, thereby preventing β-adrenergic stimulation. The mechanism of its antihypertensive and antimigraine effects is not completely understood.

Drug Characteristics: Propranolol

Dose Adjustment Hepatic	Titrate with caution	**Absorption**	F = 30-70%, food increases absorption
Dose Adjustment Renal	Titrate with caution	**Distribution**	Vd = 6 L/kg; 93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP1A2, CYP2D6 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 1% with a half-life of 3-4 h
Lactation	Compatible	**Pharmacogenetics**	Use with caution in CYP2D6 poor metabolizers
Contraindications	Hypersensitivity to propranolol; asthma; sinus bradycardia, AV block, sick sinus syndrome, cardiogenic shock	**Black Box Warnings**	Avoid abrupt withdrawal

Medication Safety Issues: Propranolol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
LA, XL	No	Extended-release formulations	Yes	Adderall, Isordil, prasugrel	No

Drug Interactions: Propranolol

Typical Agents	Mechanism	Clinical Management
CYP1A2 inducers	Increased propranolol metabolism reduces propranolol effectiveness	Consider dose increases of propranolol
CYP1A2, CYP2D6 inhibitors	Decreased propranolol metabolism increases risk of propranolol toxicity	Consider dose decreases of propranolol
NSAIDs	Decreased antihypertensive effect of propranolol	Avoid concurrent use or monitor BP
Antidiabetic drugs	Decreased glycemic control	Monitor blood glucose levels
Calcium channel blockers, alpha-blockers	Increased risk of hypotension and/or bradycardia and AV block	Avoid concurrent use, or monitor BP and HR
Digoxin	Increased risk of AV block	Monitor HR, ECG, and serum digoxin concentrations

Adverse Reactions: Propranolol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypotension	Bradyarrhythmias, bronchospasm, constipation, dizziness, dyspnea, disorder of glucose regulation, fatigue, headache, heart block, impotence, nausea, pruritus, rash, vomiting, urticaria	Heart failure, interstitial nephritis

Efficacy Monitoring Parameters. Decreased BP, chest pain, number of angina attacks, nitroglycerin use, signs/symptoms of CHF, reduction in tremors, frequency of migraines.

Toxicity Monitoring Parameters. Signs/symptoms of CHF, decreased HR, bronchospasm, increased FPG, exacerbations of angina pectoris, or acute coronary insufficiency. Monitor HR and BP.

Key Patient Counseling Points. Take immediate-release tablets on an empty stomach; ER can be taken with or without food but consistently. Avoid alcohol. Avoid abrupt discontinuation; exacerbations of angina may occur. Report signs/symptoms of hypotension, CHF, or exacerbation of angina with initial dosing and dose changes. This medicine may cause dizziness. Diabetic patients should carefully follow blood glucose as beta-blockers may mask symptoms of hypoglycemia.

Clinical Pearls. When discontinuance of propranolol is planned, dosage should be gradually reduced. Avoid in patients with poorly controlled asthma or bronchospasm as beta-blockade may exacerbate symptoms. Consider cardioselective beta-blocker as an alternative.

QUETIAPINE: Seroquel, Seroquel XR, Various

Class: Antipsychotic (Atypical)

Dosage Forms. **Oral Tablet:** 25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg; **Oral Tablet, Extended Release:** 50 mg, 150 mg, 200 mg, 300 mg, 400 mg

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disorder or schizophrenia, therapy initiation: Adults, immediate release, 50 mg po bid × 1 d, increase 50 mg/d × 3 d, may titrate to 800 mg/d; Adults, extended release, 300 mg po hs × 1 d, then 600 mg po hs × 1 d, may titrate to 800 mg/d; Children 10-17 y of age, immediate release, 50 mg po × 1 d, then 100 mg po × 1 d, then 200 mg po × 1 d, then 300 mg po × 1 d, then 400 mg po × 1 d, may titrate to 600 mg/d
2. Bipolar disorder or schizophrenia, maintenance: Adults, immediate release: 400-800 mg/d po; Adults, extended release, 400-800 mg/d po; Children 10-17 y of age, regular release, titrate to lowest effective dose
3. Major depressive disorder: Adults, extended release, 50 mg po daily hs, may titrate to 300 mg/d

Off-Label Uses.

1. Delirium in the critically ill: Adults, extended release, 50 mg po daily hs, may titrate to 300 mg/d
2. **MOA.** Quetiapine is an antagonist at multiple neurotransmitter receptors in the brain. It antagonizes serotonin 5-HT_{1A} and 5-HT_2, dopamine D_1 and D_2, histamine H_1, and adrenergic α_1 and α_2 receptors. Efficacy in schizophrenia and bipolar disorder is due to the antagonism of a combination of D_2 and 5-HT_2 receptors. Quetiapine also has no affinity for cholinergic muscarinic and benzodiazepine receptors.

AstraZeneca pictured

Drug Characteristics: Quetiapine

Dose Adjustment Hepatic	Regular release, initiate at 25 mg po daily; extended release, initiate at 50 mg po daily	**Absorption**	F = 9%, Cmax and AUC of extended-release tablet increased by high-fat meal
Dose Adjustment Renal	Not required	**Distribution**	Vd = 6-14 L/kg; 83% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 73% with a half-life of 6-7 h
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to quetiapine, drugs that increase QT interval	**Black Box Warnings**	Mortality in elderly with dementia, suicidality, not approved for children <10 y

Medication Safety Issues: Quetiapine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	QUEtiapine, SEROquel	XR formulation	No	OLANZapine, SINEquan	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others

Drug Interactions: Quetiapine

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased quetiapine metabolism reduces quetiapine effectiveness	Consider dose increases of quetiapine
CYP3A4/5 inhibitors	Decreased quetiapine metabolism increases risk of quetiapine toxicity	Consider dose decreases of quetiapine
Agents that increase QT interval	Increased risk of QT prolongation (torsades de pointes, cardiac arrest)	Use with caution in combination with other agents that may prolong QTc; avoid in congenital long QT syndrome

Adverse Reactions: Quetiapine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Agitation, headache, hypertension, somnolence, weight gain, xerostomia	Abdominal pain, asthenia, anxiety, backache, cataracts, constipation, dizziness, extrapyramidal effects, fatigue, hyperglycemia, hyperlipidemia, hyperprolactinemia, increased appetite, indigestion, insomnia, lethargy, nasal congestion, nausea, orthostatic hypotension, rash, tachycardia, tremor, vomiting	Neuroleptic malignant syndrome, neutropenia, pancreatitis, sudden cardiac death, syncope, tardive dyskinesia

Efficacy Monitoring Parameters. Improvement in signs and symptoms of schizophrenia, manic or mixed episodes associated with bipolar disorder, depression.

Toxicity Monitoring Parameters. BP, FPG, and CBC with differential, eye examination at baseline and periodically during therapy; fasting lipid profile/HgA_{1c} at baseline, 3 mo, and annually; weight, growth, BMI; TSH/T4; patients at high risk for suicide should be closely supervised.

Key Patient Counseling Points. Take with food but avoid alcohol. Avoid activities requiring mental alertness or coordination. Use caution with activities leading to an increased core temperature. Rise slowly from a sitting/supine position. Report signs/symptoms of hyperglycemia, bradycardia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome.

Clinical Pearls. Regular release may be switched to extended release at the equivalent total daily dose taken once daily; individual dosage adjustments may be required. Elderly patients with dementia-related psychosis taking quetiapine are at an increased risk of death compared to placebo.

QUINAPRIL: Accupril, Various

Class: ACE-I, Antihypertensive

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: 5 mg po bid, may titrate to 20-40 mg po bid
2. Hypertension: 10-20 mg po daily, may titrate to 80 mg po daily

Off-Label Uses.

1. Diabetic nephropathy: 20-40 mg po daily

MOA. Quinapril is a competitive ACE-I; it prevents conversion of angiotensin I to angiotensin II (a vasoconstrictor). It also reduces serum aldosterone leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system and alters prostanoid metabolism, inhibits sympathetic nervous system, and inhibits the tissue renin–angiotensin system.

Greenstone 10 mg generic pictured

Drug Characteristics: Quinapril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%, food decreases rate and extent of absorption
Dose Adjustment Renal	CrCl 30-60 mL/min, 5 mg po daily; CrCl 10-30 mL/min, 2.5 mg po daily	**Distribution**	Vd = 0.7 L/kg; 97% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic to active metabolite (quinaprilat) but not via CYP450
Pregnancy Category	D	**Elimination**	Renal elimination is 50-60% with a half-life of 25 h (metabolite)
Lactation	Weigh risks and benef ts	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to quinapril or other ACE-Is, history of ACE-I–induced angioedema	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Quinapril

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	AcipHex, Accutane	No

Drug Interactions: Quinapril

Typical Agents	Mechanism	Clinical Management
Antacids	Binding and decreased absorption of quinapril	Separate administration by 2 h
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Angiotensin receptor blockers	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive effect of quinapril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels
Aliskiren	Increased risk of hyperkalemia	Monitor serum potassium levels
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use; monitor for anemia or leukopenia
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly

Adverse Reactions: Quinapril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, dizziness, dry cough, fatigue, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting	Angioedema, birth defects, liver failure

Efficacy Monitoring Parameters. BP, signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of angioedema, persistent dry cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

Key Patient Counseling Points. Avoid pregnancy. Avoid sudden discontinuation; rebound hypertension can occur. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

Clinical Pearls. Safety and efficacy not established in children (captopril and enalapril are more commonly used in children). The full effect may not be observed for 2-4 wk. Dry cough associated with ACE-I is typically a class effect; consider switching to an ARB. Can lead to increases in SCr and potassium; recheck electrolytes within a week of initiation.

RABEPRAZOLE: AcipHex

Class: Proton Pump Inhibitor

Dosage Forms. **Oral Tablet, Delayed Release:** 20 mg; **Oral Capsule, Oral Sprinkle**: 20 mg

Common FDA Label Indication, Dosing, and Titration.

1. Duodenal ulcer disease: 20 mg po daily × up to 4 wk
2. *H. pylori* GI infection: 20 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
3. Gastric hypersecretion: 60 mg po daily, may titrate to 60 mg po bid
4. GERD, erosive or ulcerative, for symptom control, initial treatment, or maintenance: Adults and Children >12 y of age, 20 mg po daily

Eisai 20 mg pictured

Off-Label Uses.

1. Drug-induced GI disturbance, indigestion: 20 mg po daily
2. Gastric ulcer disease: 20-40 mg po daily

MOA. Rabeprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to H^+/K^+-ATPase (proton pump), which is the final pathway for acid secretion. Rabeprazole produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, and pentagastrin- and food-stimulated gastric acid secretion.

Drug Characteristics: Rabeprazole

Dose Adjustment Hepatic	Required for hepatic dysfunction	**Absorption**	F = 52%, food delays absorption
Dose Adjustment Renal	Not required	**Distribution**	96% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, substrate for CYP3A4/5, 2C19; moderate inhibitor of CYP2C8
Pregnancy Category	B	**Elimination**	Renal elimination is 90% with a half-life of 1-2 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2C19 poor metabolizers have greater gastric acid suppression
Contraindications	Hypersensitivity to rabeprazole	**Black Box Warnings**	None

Medication Safety Issues: Rabeprazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	RABEprazole	Do not crush tablets, sprinkle capsules may be opened but not chewed	No	Aricept, ARIPiprazole	No

Drug Interactions: Rabeprazole

Typical Agents	Mechanism	Clinical Management
CYP3A4/5, 2C19 inducers	Increased rabeprazole metabolism reduces rabeprazole effectiveness	Monitor and consider dose increases of rabeprazole
CYP3A4/5, 2C19 inhibitors	Decreased rabeprazole metabolism increases risk of rabeprazole toxicity	Monitor and consider dose decreases of rabeprazole
CYP2C8 substrates	Decreased substrate metabolism may result in substrate toxicity	Monitor and consider decreasing dose of substrate
pH-dependent drugs	Lower gastric pH reduces absorption	Monitor pH-dependent drug and adjust dose as necessary
Clopidogrel	May decrease the effect of clopidogrel on platelet inhibition, resulting in cardiovascular events (MI, stroke, death)	Avoid concurrent use; consider alternative acid-reducing agent such as H_2 inhibitor
Warfarin	Increased INR and risk of bleeding	Monitor INR and consider dose adjustment

Adverse Reactions: Rabeprazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Headache, rash	Stevens-Johnson syndrome, fracture of bone, rhabdomyolysis, acute interstitial nephritis

Efficacy Monitoring Parameters. Resolution of GI symptoms, (reflux, ulcers, *H. pylori*, infection)

Toxicity Monitoring Parameters. Headache, SCr or blistering skin rash.

Key Patient Counseling Points. Open sprinkle capsules into a small quantity of room-temperature soft food or liquid and administer within 15 min. If used for duodenal ulcers, administer with breakfast.

Clinical Pearls. Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; patients should complete full regimen if prescribed for *H. pylori* management. Many PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Possible increased risk of osteoporosis. Use for shortest period of time and avoid use in those at risk for osteoporosis if possible.

RALOXIFENE: Evista

Class: Selective Estrogen Receptor Modulator

Dosage Forms. Oral Tablet: 60 mg

Lilly 60 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Breast cancer, invasive, in postmenopausal women at high risk; prophylaxis: 60 mg po daily
2. Postmenopausal osteoporosis, prevention or treatment: 60 mg po daily

Off-Label Uses. None

MOA. Raloxifene is a selective estrogen receptor modulator (SERM) and binds to estrogen receptors, resulting in activation of estrogenic pathways in some tissues (agonism) and blockade of estrogenic pathways in others (antagonism). Raloxifene appears to act as an estrogen agonist in bone, decreasing bone resorption and bone turnover and increasing BMD.

Drug Characteristics: Raloxifene

Dose Adjustment Hepatic	Not required	**Absorption**	F = 2%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2583 L/kg; 95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic; not via CYP
Pregnancy Category	X	**Elimination**	Fecal elimination with a half-life of 32 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to raloxifene; pregnancy or lactation, current or history of thromboembolic disorders	**Black Box Warnings**	Venous thromboembolism, stroke

Medication Safety Issues: Raloxifene

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	AVINza	No

Drug Interactions: Raloxifene

Typical Agents	Mechanism	Clinical Management
Bile acid sequestrants	Reduced absorption of raloxifene	Avoid concurrent use

Adverse Reactions: Raloxifene

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hot f ashes, arthralgia, f u-like symptoms	Rash, sweating, weight gain, f atulence, nausea, vaginitis, bronchitis	Edema, hypertriglyceridemia venous thrombo-embolism, cerebrovascular accident, pulmonary embolism

Efficacy Monitoring Parameters. DEXA scan (BMD), mammogram.

Toxicity Monitoring Parameters. Weight gain, shortness of breath, symptoms of stroke, DVT (swelling of the leg, redness, pain); triglycerides.

Key Patient Counseling Points. Raloxifene increases the risk of blood clots, especially during the first 4 mo of therapy. Avoid sitting for long periods and be aware of the symptoms of DVT. If taking for osteoporosis, consider calcium and vitamin D supplementation.

Clinical Pearls. Tamoxifen and raloxifene are equivalent in efficacy of preventing breast cancer; however, raloxifene causes less endometrial hyperplasia, thromboembolic events, and cataracts. Medication guide required at dispensing.

RALTEGRAVIR: Isentress

Class: Antiretroviral Agent, Integrase Inhibitor

Dosage Forms. Oral Tablet: 400 mg; **Oral Chewable Tablet:** 25 mg; 100 mg; **Powder for Oral Suspension:** 100 mg/packet

Merck 400 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Treatment of HIV-1 infection in combination with other antiretroviral agents: Adults and Children ≥12 y of age, 400 mg po bid; Children <12 y of age, dose is weight based

Off-Label Uses.

1. Occupational HIV postexposure prophylaxis: 400 mg po bid with concomitant emtricitabine/tenofovir

MOA. Raltegravir inhibits the catalytic activity of integrase HIV-1 integrase, thus preventing integration of the proviral gene into human DNA.

Drug Characteristics: Raltegravir

Dose Adjustment Hepatic	Use with caution if severe hepatic impairment	**Absorption**	F = 30-40%, no food effect
Dose Adjustment Renal	Not required	**Distribution**	CSF, semen
Dialyzable	No	**Metabolism**	Metabolized by UGT1A1 to an inactive metabolite
Pregnancy Category	C	**Elimination**	50% of the metabolites in feces, 30% renally eliminated as parent, half-life 9-12 h
Lactation	Weight risks and benefits	**Pharmacogenetics**	Resistance is associated with HIV mutations
Contraindications	None	**Black Box Warnings**	None

Medication Safety Issues: Raltegravir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew or crush oral tablets	Yes	No	No

Drug Interactions: Raltegravir

Typical Agents	Mechanism	Clinical Management
Aluminum salt, magnesium salts	Decreased absorption of raltegravir	Contraindicated
Fosamprenavir	Decreased amprenavir concentrations, unknown mechanism	Avoid
PPIs and H_2-blockers	Increased absorption of raltegravir with increased pH	Monitor for toxicity and consider dose reductions of raltegravir
Rifampin	Decreased raltegravir via induction of UGT by rifampin	Increase raltegravir dose to 800 mg bid

Adverse Reactions: Raltegravir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Hyperglycemia, insomnia, headache, neutropenia, elevated LFTs	Anemia, cerebellar ataxia, depression, hepatitis, hypersensitivity, myopathy, nephrolithiasis, psychomotor hyperactivity (children), renal failure, rhabdomyolysis, Stevens-Johnson syndrome, suicidal ideation/behavior, thrombocytopenia, toxic epidermal necrolysis

Efficacy Monitoring Parameters. HIV viral load, CD4 count, HIV resistance testing.

Toxicity Monitoring Parameters. LFTs, bilirubin, CBC, glucose.

Key Patient Counseling Points. Take with or without food. May chew or crush the chewable tablet. For the oral suspension, add contents of foil pack (100 mg) to 5 mL water and swirl for 30-60 s. Use oral syringe to obtain correct dose. Administer within 30 min. Does not prevent transmission of HIV; practice safe sex.

Clinical Pearls. Not recommended for children <2 y of age. Recommended as a first-line therapy with tenofovir/emtricitabine in antiretroviral naïve patients. Chewable tablet and oral suspension have higher bioavailability than oral tablet; do not interchange these products.

RAMIPRIL: Altace, Various

Class: ACE-I, Antihypertensive

Dosage Forms. **Oral Capsule:** 1.25 mg, 2.5 mg, 5 mg, 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure post-MI: 1.25-2.5 mg po bid × 7 d, may titrate to 5 mg po bid
2. Hypertension: 2.5 mg po daily, may titrate to 2.5-20 mg po daily
3. Reduce risk of myocardial infarction, stroke and death from cardiovascular causes: 2.5 mg po bid × 7 d, may titrate as tolerated to 10 mg daily.

Off-Label Uses.

1. Diabetic nephropathy, kidney disease: 1.25-10 mg po daily

MOA. Ramipril is a competitive ACE-I. It is also a prodrug for the more potent ACE-I ramiprilat. ACE-I prevents conversion of angiotensin I to angiotensin II (a vasoconstrictor). It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and inhibits the tissue renin–angiotensin system.

Lupin generic 10 mg pictured

Drug Characteristics: Ramipril

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%, food has no effect on absorption
Dose Adjustment Renal	CrCl <40 mL/min: use 25% of normal dose	**Distribution**	73% protein bound
Dialyzable	Yes	**Metabolism**	Metabolized in liver to active metabolite (ramiprilat) not via CYP
Pregnancy Category	C (1st trimester), D (2nd and 3rd trimesters)	**Elimination**	Renal elimination is 50-60% with a half-life of 13-17 h (metabolite)
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ramipril or other ACE-Is, history of ACE-I–induced angioedema	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Ramipril

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Capsule	No	Amaryl, enalapril	No

Drug Interactions: Ramipril

Typical Agents	Mechanism	Clinical Management
Antacids	Binding and decreased absorption	Separate administration by 2 h
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Angiotensin receptor blockers	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive effect of ramipril, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr levels
Aliskiren	Increased risk of hyperkalemia	Monitor serum potassium levels
Azathioprine	Increased risk of myelosuppression	Avoid concurrent use; monitor for anemia or leukopenia
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly

Adverse Reactions: Ramipril

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Diarrhea, dizziness, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting	Angioedema, birth defects, liver failure

Efficacy Monitoring Parameters. BP, progression of heart failure.

Toxicity Monitoring Parameters. Angioedema (swelling of the face, eyes, lips, tongue, or throat), persistent dry cough, hypotension; baseline and periodic potassium, SCr, BUN, and urine protein.

Key Patient Counseling Points. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

Clinical Pearls. Contents of capsule may be mixed with water, apple juice, or apple sauce for administration but do not chew. Dry cough associated with ACE-I is typically a class effect; consider switching to an ARB. Can lead to increases in SCr and K^+; recheck electrolytes within 1 wk of initiation.

RANITIDINE: Zantac, Various

Class: Histamine H_2 Receptor Antagonist

Dosage Forms. Oral Tablet: 75 mg, 150 mg, 300 mg; **Oral Capsule:** 150 mg, 300 mg; **Oral Syrup:** 15 mg/mL; **Oral Suspension:** 22.4 mg/mL

Amneal generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Duodenal ulcer, acute or maintenance, gastric ulcer, acute or maintenance, erosive esophagitis, acute or maintenance: Children 1 mo to 16 y of age, 2-4 mg/kg po bid, *max* of 300 mg/d; Adults, 150 mg po bid or 300 mg po daily hs
2. Indigestion, prevention or treatment: 75-150 mg po bid
3. *H. pylori* GI tract infection, quadruple therapy: 150 mg po bid × 10-14 d in combination with metronidazole 250 mg po qid, bismuth subsalicylate 525 mg po qid, and tetracycline 500 mg po qid

Off-Label Uses.

1. Stress ulcer prophylaxis: 150 mg po bid

MOA. Ranitidine competitively inhibits histamine H_2 receptors and inhibits gastric acid secretion. Both the acid concentration and volume of gastric secretion are suppressed by ranitidine, while changes in pepsin secretion are proportional to volume output.

Drug Characteristics: Ranitidine

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50%, food has no effect on absorption
Dose Adjustment Renal	CrCl <50 mL/min, *max* of 150 mg po daily	**Distribution**	Vd = 1.4 L/kg; 15% protein bound
Dialyzable	Yes	**Metabolism**	Minor hepatic, not via CYP
Pregnancy Category	B	**Elimination**	Renal elimination is 30-70% with a half-life of 2-3 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ranitidine or other H_2 antagonists	**Black Box Warnings**	None

Medication Safety Issues: Ranitidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
FusePaq, Maximum strength	No	No	No	Xanax, Zofran, Zyrtec	No

Drug Interactions: Ranitidine

Typical Agents	Mechanism	Clinical Management
pH-dependent drugs	Lower gastric pH reduces absorption	Separate administration by 12 h or use alternative agents

Adverse Reactions: Ranitidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, diarrhea, nausea	Skin rash	Stevens-Johnson syndrome, increased liver enzymes, acute interstitial nephritis

Efficacy Monitoring Parameters. Resolution of GERD symptoms, resolution of peptic ulcers, gastric pH (if indicated).

Toxicity Monitoring Parameters. SCr, AST, ALT

Key Patient Counseling Points. Advise patients to take at bedtime. Patients may take with food or antacids, if needed.

Clinical Pearls. This and other PPI and H_2 antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Injectable dosage form also available; when the intravenous route is used, treatment should be converted to oral route as soon as possible to avoid cost and risks associated with intravenous therapy. If taking as needed to prevent heartburn, take 30-60 min before problem foods.

RANOLAZINE: Ranexa

Class: Antianginal agent

Dosage Forms. **Oral Tablet, Extended Release:** 500 mg, 1000 mg

Common FDA Label Indication, Dosing, and Titration.

1. Chronic angina: Initial, 500 mg po bid, may titrate to *max* dose 1000 mg po bid

Off-Label Uses. None

MOA. Ranolazine inhibits the late phase of the inward sodium channel during cardiac repolarization reducing intracellular sodium concentrations and thereby reducing calcium influx via Na^{+}-Ca^{2+} exchange that in turn reduces ventricular tension and myocardial oxygen consumption.

Drug Characteristics: Ranolazine

Dose Adjustment Hepatic	Avoid if severe hepatic dysfunction	**Absorption**	F = 76%, food has no effect on absorption
Dose Adjustment Renal	Avoid if acute renal failure	**Distribution**	62% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate, P-glycoprotein substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 75% with a half-life of 7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hepatic cirrhosis, strong CYP3A4 inducers or inhibitors	**Black Box Warnings**	None

Medication Safety Issues: Ranolazine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew, crush, or break	No	CeleXA	No

Drug Interactions: Ranolazine

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased ranolazine metabolism reduces ranolazine effectiveness	Strong inducers contraindicated. Moderate or weak inducers; monitor and consider dose increase of ranolazine
CYP3A4/5 inhibitors	Decreased ranolazine metabolism increases risk ranolazine toxicity	Strong inhibitors contraindicated. *Max* dose is 500 mg bid if concurrent strong inhibitors
P-glycoprotein inducers	Increased ranolazine transport reduces ranolazine effectiveness	Monitor and consider dose increase of ranolazine
P-glycoprotein inhibitors	Decreased ranolazine transport increases risk ranolazine toxicity	Contraindicated
Agents that prolong the QTc interval	Additive QTc prolongation	Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome

Adverse Reactions: Ranolazine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dizziness, headache, bradycardia, hypotension, edema, constipation, nausea, xerostomia, blurred vision	Angioedema, pancytopenia, pulmonary fibrosis, arrhythmia, renal failure, syncope, QTc prolongation

Efficacy Monitoring Parameters. Improvement in angina symptoms, improved exercise tolerance.

Toxicity Monitoring Parameters. Baseline and follow-up ECG to evaluate QTc if concerns for prolongation, monitor BP and renal function at baseline and periodically.

Key Patient Counseling Points. Do not crush or chew, but may be taken with or without meals. There are multiple significant drug interactions so talk to pharmacist or physician before starting any new medications or herbal supplements. Ranolazine will not stop an acute angina episode.

Clinical Pearls. May be used in combination with beta-blockers or alone in patients who do not respond to or tolerate beta-blockers.

REPAGLINIDE: Prandin

Class: Meglitinide, Antidiabetic

Dosage Forms. Oral Tablet: 0.5 mg, 1 mg, 2 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus, type 2: 0.5-4 mg po bid-qid (with meal), may titrate to 16 mg po daily

Off-Label Uses. None

MOA. Repaglinide is a meglitinide agent that stimulates insulin release from the pancreas via inhibition of adenosine triphosphate (ATP)-potassium channels on the beta-cell membrane and potassium efflux. The resulting depolarization and calcium influx induces insulin secretion.

Novo Nordisk 2 mg pictured

Drug Characteristics: Repaglinide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 56%, food has no effect on absorption
Dose Adjustment Renal	CrCl 20-40 mL/min: initial dose of 0.5 mg po daily and titrate carefully	**Distribution**	Vd = 24-31 L; 98% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic substrate of CYP3A4/5, 2C8
Pregnancy Category	C	**Elimination**	Fecal elimination is 90% with a half-life of 1 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to repaglinide, diabetic ketoacidosis, type 1 diabetes, concurrent gemfibrozil	**Black Box Warnings**	None

Medication Safety Issues: Repaglinide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Avandia	No

Drug Interactions: Repaglinide

Typical Agents	Mechanism	Clinical Management
Beta-blockers, SSRIs, NSAIDs, MAOI	Altered glucose metabolism and increased risk of hypoglycemia	Monitor carefully and manage as appropriate
CYP2C8, CYP3A4/5 inducers	Increased repaglinide metabolism reduces repaglinide effectiveness	Monitor and consider dose increases of repaglinide
CYP2C8, CYP3A4/5 inhibitors	Decreased repaglinide metabolism increases risk of repaglinide toxicity	Monitor and consider dose decreases of repaglinide

Adverse Reactions: Repaglinide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypoglycemia, headache	Arthralgia nasopharyngitis, nausea, diarrhea, chest pain	Angina, hypertension, arrhythmia, thrombocytopenia, hypersensitivity, hepatotoxicity, Stevens-Johnson syndrome

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbC_{1c} <7%.

Toxicity Monitoring Parameters. Hypoglycemia (symptoms include nausea, sweating, loss of consciousness, mental status changes, nervousness, headache, shaking, and seizures). Monitor BP, HR, CBC, and LFT.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times/d). Take 15-30 min before each meal, up to 4 times/day. Do not take if skipping a meal. Add a dose if eating an extra meal. Counsel on recognition and treatment of hypoglycemia. Encourage healthy lifestyle choices to improve glucose control.

Clinical Pearls. Compared with sulfonylureas, repaglinide has a quicker onset and shorter duration of action, resulting in a lower risk of prolonged hypoglycemia. No studies evaluate use in children; avoid. Repaglinide is usually considered a third-line therapy for type 2 diabetes, but could be first-line therapy in patients with contraindications to metformin (impaired renal function) or intolerance to sulfonylureas. Also available as combination tablet with metformin. Use caution in combination with beta-blockers, which can mask hypoglycemia.

RISEDRONATE: Actonel, Atelvia

Class: Bisphosphonate

Dosage Forms. **Oral Tablet:** 5 mg, 30 mg, 35 mg, 150 mg; **Oral Tablet, Delayed Release:** 35 mg

Common FDA Label Indication, Dosing, and Titration.

1. Postmenopausal osteoporosis: Delayed release, 35 mg po once weekly immediately following breakfast; immediate release, 5 mg po daily, 35 mg po once weekly, or 150 mg po once a month; all with supplemental calcium and vitamin D
2. Paget disease: Immediate release, 30 mg po daily for 2 mo
3. Osteoporosis (glucocorticoid induced) prevention and treatment: Immediate release, 5 mg po daily
4. Osteoporosis (male): Immediate release, 35 mg po once weekly

Off-Label Uses. None

MOA. Risedronate binds to bone hydroxyapatite and inhibits osteoclast activity at the cellular level, thereby modulating bone metabolism.

Procter & Gamble
35 mg pictured

R

Drug Characteristics: Risedronate

Dose Adjustment Hepatic	Not required	**Absorption**	F <1%, food impairs absorption, take 30-60 min prior to meal
Dose Adjustment Renal	CrCl <30 mL/min, avoid	**Distribution**	Vd = 13.8 L; 24% protein bound
Dialyzable	Unknown	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 50% with a half-life of 561 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Known hypersensitivity to risedronate, esophageal abnormalities that delay esophageal emptying, hypocalcemia, inability to sit or stand upright for at least 30 min	**Black Box Warnings**	None

Medication Safety Issues: Risedronate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew or crush either formulation	No	Alendronate, Actos	No

Drug Interactions: Risedronate

Typical Agents	Mechanism	Clinical Management
Aluminum, calcium-containing products	Decreased bisphosphonate absorption	Separate administration by 1-2 h
H_2-blockers and PPIs	Decreased bisphosphonate absorption	Separate administration by 12 h, avoid XR formulation

Adverse Reactions: Risedronate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Rash, abdominal pain, constipation, diarrhea, nausea, indigestion, backache, UTI	Asthenia, flu-like illness, edema, arrhythmias, nephrolithiasis, myalgia, bone pain	Osteonecrosis of the jaw, hypersensitivity reaction

Efficacy Monitoring Parameters. Increased BMD, decreased incidence of fractures, normalization of alkaline phosphatase (Paget's).

Toxicity Monitoring Parameters. Baseline SCr, calcium. Severe skin rash, chest pain, difficulty in swallowing, swelling, tooth problems, pain with urination, severe pain.

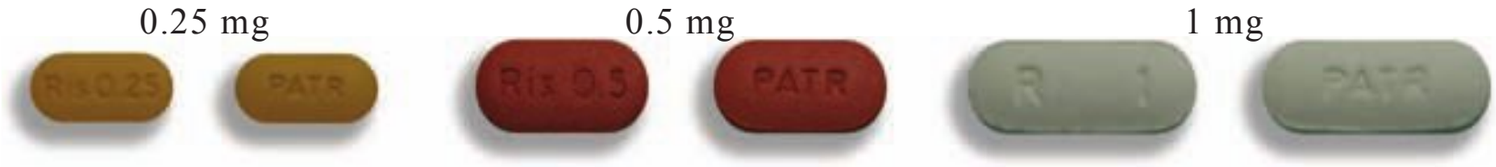
Key Patient Counseling Points. Take as soon as you get out of bed in the morning, before you eat or have anything to drink. Swallow tablet whole with 240 mL of plain water only (not mineral water, coffee, juice, or any other liquid). Do not chew tablet. Do not take the medicine while you are still in bed, and do not take it at bedtime. Wait at least 30 min after you swallow the tablet before you eat or drink anything or take any other medicines. Do not lie down for at least 30 min after taking this medicine, and do not lie down until after you have eaten some food.

Clinical Pearls. Concurrent chemotherapy and poor oral hygiene increase the risk for osteonecrosis of the jaw. Atypical fractures of the thigh (subtrochanteric and diaphyseal femur fractures) have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Atelvia is the brand name of the extended-release product. Medication guide required at dispensing.

RISPERIDONE: Risperdal, Various

Class: Benzisoxazole, Antipsychotic

Dosage Forms. Oral Tablet: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg; **Oral Dispersible Tablet:** 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg; **Oral Solution:** 1 mg/mL



Common FDA Label Indication, Dosing, and Titration.

1. Autistic disorder, irritability: Children ≥5 y of age and weighing <20 kg, 0.25 mg po daily, titrate to response; Children ≥5 y of age and weighing >20 kg, 0.5 mg po daily, titrate to response
2. Bipolar I disorder: Adults, 2-3 mg po daily, may titrate to 6 mg/d; Children ≥10 y of age, 0.5 mg po daily, may titrate to 2.5 mg/d
3. Schizophrenia: Adults, 1 mg po bid, may titrate to 18 mg/d; Children ≥13 y of age, 0.5 mg po daily, may titrate to 3 mg/d

Off-Label Uses.

1. Posttraumatic stress disorder: 0.5-8 mg po once daily
2. Tourette syndrome: 0.25-0.5 mg po daily, may titrate to *max* dose of 6mg po daily
3. Pervasive developmental disorder: Children ≥5 y of age, 0.01 mg/kg/dose po daily, may titrate to 0.06 mg/kg/d

MOA. Risperidone is a potent serotonin-5-HT_2 antagonist with weaker dopamine-D_2 antagonism. Whereas typical antipsychotics are dopamine antagonists, the additional serotonin antagonism increases efficacy for negative symptoms of schizophrenia and reduces the likelihood of extrapyramidal symptoms.

Drug Characteristics: Risperidone

Dose Adjustment Hepatic	Severe hepatic impairment, initiate at 0.5 mg po bid, titrate slowly	**Absorption**	F = 70%, food has no effect on absorption
Dose Adjustment Renal	Severe renal impairment, initiate at 0.5 mg po bid, titrate slowly	**Distribution**	Vd = 1-2 L/kg; 90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, substrate of CYP2D6, to active metabolite (9-hydroxyrisperidone), P-glycoprotein substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 3-20 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 poor metabolizers have higher risperidone and lower metabolite levels; limited clinical implication as both parent and metabolite are active
Contraindications	Hypersensitivity to risperidone, agents that increase QT interval	**Black Box Warnings**	Mortality in elderly with dementia

Medication Safety Issues: Risperidone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Consta, M-Tab	RisperiDONE, RisperDAL	Dispersible tablet	No	Reserpine, rOPINIRole	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others

Drug Interactions: Risperidone

Typical Agents	Mechanism	Clinical Management
CYP2D6, P-glycoprotein inhibitors	Decreased risperidone metabolism increases risk of risperidone toxicity	Monitor and consider dose decreases of risperidone; *max* dose 8 mg/d in combination w/fluoxetine or paroxetine
P-glycoprotein inducers	Increased risperidone excretion reduces risperidone effectiveness	Monitor and consider dose increases of risperidone
Agents that increase QT interval	Increased risk of QT prolongation (torsades de pointes, cardiac arrest)	Use with caution in combination with other agents that may prolong QTc; avoid in congenital long QT syndrome
Valproic acid	Increased valproic acid concentrations	Monitor for adverse effects, monitor valproic acid serum levels, adjust dose as needed
Anticholinergics	Additive anticholinergic activity	Avoid combination

Adverse Reactions: Risperidone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Extrapyramidal symptoms, insomnia, anxiety, fatigue, metabolic changes (hyperglycemia, dyslipidemia, weight gain, DM)	Abdominal pain, akathisia, GI symptoms (constipation, N/V, diarrhea, dyspepsia), cough, dizziness, hyperprolactinemia, orthostatic hypotension, edema, rash, rhinitis, tachycardia, tremor, xerostomia, dysphagia	Neuroleptic malignant syndrome, pancreatitis, stroke, pancytopenia, sudden cardiac death, syncope, tardive dyskinesia, priapism

Efficacy Monitoring Parameters. Improvement in signs and symptoms of schizophrenia, manic or mixed episodes associated with bipolar disorder, depression.

Toxicity Monitoring Parameters. BP (including orthostatics), FPG, A1C in diabetic patients, lipid panel, weight, BMI, abdominal circumference, CBC w/differential, symptoms of tardive dyskinesia; closely supervise patients at high risk for suicide.

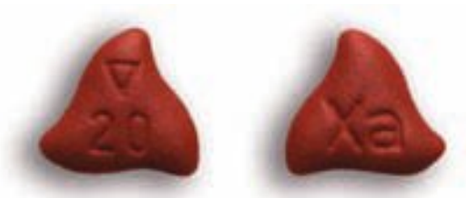
Key Patient Counseling Points. Take with food. Avoid alcohol or other CNS depressants. Avoid activities requiring mental alertness or coordination until drug effects are known. Use caution during activities leading to an increased core temperature. Rise slowly from a sitting/supine position. Report signs/symptoms of hyperglycemia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome. Keep dispersible tablet in blister pack until use. Place on tongue and swallow after dissolved. Oral solution may be mixed with water, coffee, orange juice, or low fat milk, but should not be mixed with cola or tea.

Clinical Pearls. Monitor closely for tardive dyskinesia; tics may become permanent if not treated appropriately. Increases risk of death in elderly patients with dementia-related psychosis. If initiating Risperdal CONSTA (IM injection Q2 wk), continue oral antipsychotic for 3 wk after 1st injection, then discontinue.

RIVAROXABAN: Xarelto

Class: Anticoagulant, Factor Xa inhibitor

Dosage Forms. Oral Tablet: 10 mg, 15 mg, 20 mg



Janssen 20 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of thromboembolism in patients after orthopedic surgery: 10 mg po daily beginning at least 6 h after surgery × 12-14 d for knee replacement or 35 d for hip replacement; if CrCl 30-50 mL/min no dose adjustment, use with caution; do not use if CrCl <30 mL/min
2. Prevention of thromboembolism in patients with nonvalvular atrial fibrillation: 20 mg po daily if CrCl >50 mL/min; 15 mg po daily if CrCl 15-50 mL/min; do not use if CrCl <15 mL/min
3. Treatment and secondary prevention of DVT or pulmonary embolism: 15 mg po bid × 21 d, then 20 mg po daily; do not use if CrCl <30 mL/min

Off-Label Uses. None

MOA. Rivaroxaban is an orally bioavailable factor Xa inhibitor that selectively blocks the active site of factor Xa and does not require a cofactor (such as anti-thrombin III) for activity. Activation of factor X to factor Xa via the intrinsic and extrinsic pathways plays a central role in the cascade of blood coagulation.

Drug Characteristics: Rivaroxaban

Dose Adjustment Hepatic	Avoid use in moderate to severe dysfunction	**Absorption**	F = 66-100%; food increases extent of absorption at higher doses
Dose Adjustment Renal	Dose adjustments based on indication, see above	**Distribution**	Vd = 50 L; 95% albumin bound
Dialyzable	Use in ESRD should be avoided; hemodialysis removes 60% of drug in 2-3 h	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 66% with a half-life of 5-9 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Active bleeding	**Black Box Warnings**	Premature discontinuation increases thrombotic risk, risk of spinal/epidural hematoma

Medication Safety Issues: Rivaroxaban

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Starter Pack	No	No	Yes	No	No

Drug Interactions: Rivaroxaban

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased rivaroxaban metabolism reduces rivaroxaban effectiveness	Avoid strong CYP3A/5 inducers. Monitor carefully for clotting
CYP3A4/5 inhibitors	Decreased rivaroxaban metabolism increases risk of rivaroxaban toxicity	Avoid strong CYP3A4/5 inhibitors. Monitor carefully for bleeding
Antiplatelet agents, NSAIDs, and anticoagulants	Additive risk of bleeding	Avoid concurrent use if possible or monitor carefully for bleeding

Adverse Reactions: Rivaroxaban

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bleeding	Peripheral edema, dizziness, headache, fatigue, bruising, pruritus, rash, nausea, vomiting	Syncope, major bleeding, epidural hematoma, anaphylaxis, intracranial bleeding

Efficacy Monitoring Parameters. Prevention of clotting or recurrence of clotting. Routine monitoring of anticoagulation tests is not necessary with rivaroxaban. If used, anti-Xa activity is the preferred test.

Toxicity Monitoring Parameters. Monitor for signs and symptoms of bleeding. Monitor renal function for potential dose adjustment. Monitor CBC, vital signs.

Key Patient Counseling Points. Administer with the evening meal. Educate patient on signs and symptoms of bleeding and interactions with other anticoagulant or antiplatelet medications, including OTC medications. Warn of risks of epidural (spinal) anesthesia while taking rivaroxaban.

Clinical Pearls. Detailed dosing conversion protocols to convert patients from warfarin or parenteral anticoagulants to rivaroxaban are available in the product package insert. Many drug-drug interactions; monitor concurrent drug use carefully. Tablets may be crushed and mixed with apple sauce immediately prior to administration; may mix with water for NG tube administration.

ROPINIROLE: Requip, Requip XL, Various

Class: Dopamine Agonist

Dosage Forms. Oral Tablet: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg; **Oral Tablet, Extended Release:** 2 mg, 4 mg, 6 mg, 8 mg, 12 mg

Common FDA Label Indication, Dosing, and Titration.

1. Parkinson disease: Immediate release, 0.25 mg po tid × 1 wk, then 0.5 mg po tid × 1 wk, then 0.75 mg po tid × 1 wk, then 1 mg po tid, then may titrate to 24 mg/d; extended release, 2 mg po daily × 1-2 wk, then may titrate to 24 mg/d
2. Restless legs syndrome: Immediate release only, 0.25 mg po daily hs × 2 d, then 0.5 mg po daily hs × 5 d, then 1 mg po daily × 1 wk, then 1.5 mg po daily hs for 1 wk, then 2 mg po daily hs, then may titrate to 4 mg po daily hs

Off-Label Uses. None

MOA. Ropinirole is a nonergoline dopamine agonist that has a higher specificity to D_3 than to D_2 and D_4 subtypes of dopamine receptors. The drug has a moderate affinity for opioid receptors and has insignificant effects on D_1, 5-hydroxytryptamine 1 (5-HT_1), 5-HT_2, benzodiazepine, GABA, muscarinic, α_1-, α_2-, and β-adrenoreceptors. It is suggested that ropinirole stimulates the postsynaptic D_2-type receptor found in the brain's caudate putamen in Parkinson disease.

0.25 mg

0.5 mg

1 mg

3 mg

Core Pharma generic pictured

Drug Characteristics: Ropinirole

Dose Adjustment Hepatic	Use with caution	**Absorption**	F = 45-55%, food increases Tmax and Cmax
Dose Adjustment Renal	Not required	**Distribution**	Vd = 7.5 L/kg; 40% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP1A2 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is >80% with a half-life of 6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ropinirole	**Black Box Warnings**	None

Medication Safety Issues: Ropinirole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XL	rOPINIRole	Extended-release tablets	No	RisperDAL, risperiDONE	No

Drug Interactions: Ropinirole

Typical Agents	Mechanism	Clinical Management
CYP1A2 inducers	Increased ropinirole metabolism reduces ropinirole effectiveness	Monitor and consider dose increases of ropinirole
CYP1A2 inhibitors	Decreased ropinirole metabolism increases risk of ropinirole toxicity	Monitor and consider dose decreases of ropinirole
Antipsychotics	May decrease effectiveness of antipsychotics and/or dopamine agonists	Avoid concurrent use, or monitor both agents and consider dose adjustments to one or both

Adverse Reactions: Ropinirole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, dyskinesia, nausea, orthostatic hypotension, somnolence, vomiting, hallucinations	Abdominal pain, abnormal vision, constipation, edema, fatigue, headache, increased HR, sleep attack, syncope, vomiting	Sinus node dysfunction

Efficacy Monitoring Parameters. Reduction in extrapyramidal movements, rigidity, tremor, gait disturbances; decrease in desire to move limbs.

Toxicity Monitoring Parameters. Signs/symptoms of postural hypotension, BP, CNS depression/somnolence, decreased HR, periodic dermatologic screening.

Key Patient Counseling Points. Take with food to reduce nausea. Avoid driving and other activities requiring mental alertness or coordination until drug effects are realized. Rise slowly from sitting/lying-down position. Report new onset or exacerbation of dyskinesia, changes in BP, fainting, or unusual urges. Avoid sudden discontinuation of drug. Do not drink alcohol or take other CNS depressants while using this drug.

Clinical Pearls. May switch directly from immediate-release ropinirole to extended-release; start an extended-release dose that matches most closely with the total daily immediate-release dose.

ROSIGLITAZONE: Avandia

Class: Thiazolidinedione Antidiabetic

Dosage Forms. Oral Tablet: 2 mg, 4 mg, 8 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus: 4 mg po daily or 2 mg po bid; may titrate to *max* of 8 mg daily as monotherapy or in combination with a sulfonylurea, or metformin

Off-Label Uses. None

Glaxo SmithKline 4 mg pictured

MOA. Rosiglitazone is a thiazolidinedione antihyperglycemic and a potent peroxisome proliferator-activated receptor-gamma (PPAR [γ]) agonist used to improve insulin sensitivity in patients with type 2 diabetes. Insulin-dependent glucose disposal in skeletal muscle is improved and hepatic glucose production is decreased; both actions contribute to rosiglitazone's glucose-lowering effects.

Drug Characteristics: Rosiglitazone

Dose Adjustment Hepatic	Avoid in active liver disease or if LFT elevated	**Absorption**	F = 99%, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 17.6 L; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2C8 substrate, moderate inhibitor of CYP2C8
Pregnancy Category	C	**Elimination**	Renal elimination is 64% with a half-life of 3-4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to rosiglitazone, heart failure, NYHA class III or IV	**Black Box Warnings**	Heart failure, MI risk

Medication Safety Issues: Rosiglitazone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Avalide	No

Drug Interactions: Rosiglitazone

Typical Agents	Mechanism	Clinical Management
CYP2C8 inducers	Increased rosiglitazone metabolism reduces rosiglitazone effectiveness	Monitor and consider dose increases of rosiglitazone
CYP2C8 inhibitors	Decreased rosiglitazone metabolism increases risk of rosiglitazone toxicity	Monitor and consider dose decreases of rosiglitazone
CYP2C8 substrates	Decreased substrate metabolism may result in substrate toxicity	Monitor and consider decreasing dose of substrate
Psyllium	Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent	Avoid concurrent use if possible; monitor and consider dose adjustments
Corticosteroids	May diminish or increase hypoglycemic effect of rosiglitazone	Monitor and consider rosiglitazone dose adjustment
NSAIDs, SSRIs	Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia	Avoid concurrent use if possible; monitor and consider dose adjustments
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Rosiglitazone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Edema, weight gain, increased cholesterol	Myalgia, bone fractures, sinusitis, headache	Heart failure, MI, anemia, hepatotoxicity, diabetic macular edema, hypoglycemia when used in combination with insulin or sulfonylureas

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Weight for assessment of edema, Hgb, LFTs; symptoms of hypoglycemia include nausea, sweating, and loss of consciousness; seek care for bone pain, yellowing of skin or eyes, eye pain, or shortness of breath. Eye exam.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times/d). May take without regard to food. May require several weeks for max effect.

Clinical Pearls. Causes edema, which may exacerbate underlying heart failure, use with caution. Premenopausal anovalatory individuals may resume ovulation. Not for use in children. Thiazolidinediones are as effective as metformin, but have greater risk of adverse effects, so used as second line (both as monotherapy and in combination). Rosiglitazone has more CV effects than pioglitazone, so pioglitazone is preferred in this class. Released from REMS program in May 2014.

ROSUVASTATIN: Crestor

Class: HMG-CoA Reductase Inhibitor

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hyperlipidemia: Adults, 10-20 mg po daily, may titrate to 40 mg po daily; Children 10-17 y of age, 5-20 mg po daily, may titrate to 20 mg po daily
2. Disorder of cardiovascular system, primary prophylaxis, familial hypercholesterolemia, homozygous, hypertriglyceridemia, mixed lipidemia: 10-20 mg po daily, may titrate to 40 mg po daily

Off-Label Uses. None

MOA. HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol can also decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.

Drug Characteristics: Rosuvastatin

Dose Adjustment Hepatic	Use with caution; contraindicated in active liver disease or unexplained increased LFTs	**Absorption**	F = 20%, food slows absorption
Dose Adjustment Renal	CrCl <30 mL/min, initial dose 5 mg po daily, may titrate to 10 mg po daily	**Distribution**	Vd = 134 L; 88% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal hepatic
Pregnancy Category	X	**Elimination**	Fecal elimination is 90% with a half-life of 13-20 h
Lactation	Contraindicated	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to rosuvastatin, active liver disease, pregnancy or lactation	**Black Box Warnings**	None

40 mg

20 mg

10 mg

5 mg

AstraZeneca pictured

R

Medication Safety Issues: Rosuvastatin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	atorvaSTATin	No

Drug Interactions: Rosuvastatin

Typical Agents	Mechanism	Clinical Management
Antacids	Decreased absorption of rosuvastatin	Separate coadministration by 2 h
Bile acid-binding resins	Decreased absorption of rosuvastatin	Give rosuvastatin 1 h before or 4 h after resin
Amiodarone, azole antifungals, protease inhibitors, fibrates, niacin, cyclosporine	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use, or monitor for myopathy and measure creatine kinase levels
Warfarin	Increased risk of bleeding	Monitor INR with addition or withdrawal of rosuvastatin

Adverse Reactions: Rosuvastatin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Arthralgia	Abdominal pain, asthenia, constipation, diarrhea, indigestion, headache, increased liver enzymes, influenza-like symptoms, myalgia, nasopharyngitis, nausea, pharyngitis, rhinitis	Rhabdomyolysis, tendon rupture

Efficacy Monitoring Parameters. Total cholesterol, LDL-cholesterol, and triglycerides levels; HDL-cholesterol levels.

Toxicity Monitoring Parameters. Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs should be performed at baseline, 12 wk after initiation of therapy, and every 6 mo thereafter; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

Key Patient Counseling Points. Contact prescriber immediately if pregnancy occurs while taking rosuvastatin. Do not drink alcohol. Rosuvastatin does not take the place of diet and exercise to lower cholesterol levels.

Clinical Pearls. Lipid-level assessment should be done within 4 wk following dose initiation or titration. Consider holding rosuvastatin 4-7 d before major surgery as patient is at higher risk for occurrence of rhabdomyolysis. May increase risk of diabetes.

Merck pictured

Class: Vaccine, Live, Viral

Dosage Forms. Suspension for Oral Administration: Monovalent attenuated human rotavirus vaccine (Rotarix), pentavalent attenuated bovine rotavirus vaccine (RotaTeq)

Common FDA Label Indication, Dosing, and Titration.

1. Prophylaxis of viral gastroenteritis due to rotavirus infection: One dose po for all infants at 2 and 4 mo of age (Rotarix, 2 doses required), or 2, 4, and 6 mo of age (RotaTeq, 3 doses required); the 1st dose should be administered between 6 and 14 wk of age; do not start the series if infant >14 wk of age; all doses should be administered at least 4 wk apart and before infant reaches 24 wk of age

Off-Label Uses. None

Drug Characteristics: Rotavirus Vaccine, Live

Pregnancy Category	C	**ADME**	None known
Lactation	Infant risk is minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to rotavirus vaccine or a component of the vaccine, severe combined immunodeficiency; Rotarix may contain latex; history of intussusception	**Black Box Warnings**	None

Medication Safety Issues: Rotavirus Vaccine, Live

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Rotarix, RotaTeq	No

Drug Interactions: Rotavirus Vaccine, Live

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression increases risk of infection caused by live virus and decreases vaccine efficacy	Defer or delay rotavirus vaccine administration until corticosteroid therapy has been discontinued
Immunosuppressing agents	Immunosuppression increases risk of infection caused by live virus and decreases vaccine efficacy	Defer or delay rotavirus vaccine administration until immunosuppressive therapy has been discontinued

Adverse Reactions: Rotavirus Vaccine, Live

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Vomiting, irritability, fever, otitis media	Diarrhea	Intussusception, anaphylaxis, seizures

Efficacy Monitoring Parameters. Prevention of viral gastroenteritis due to rotavirus infection.

Toxicity Monitoring Parameters. Fever, number of stools, abdominal pain.

Key Patient Counseling Points. Return to provider for each dose in the series. Contact a health-care provider right away if the child has diarrhea, blood in his stool, vomiting, high fever, or abdominal pain as these may be symptoms of intussusception.

Clinical Pearls. If the infant fails to swallow or vomits the vaccine dose, do not readminister the dose. Immunized infant may shed virus in stools. Hand washing after diaper changing is always recommended.

SAXAGLIPTIN: Onglyza

Class: Dipeptidyl Peptidase-4 Inhibitor, Antidiabetic

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus: 2.5-5 mg po daily

Off-Label Uses. None

MOA. Saxagliptin is a dipeptidyl peptidase-4 (DPP-4) enzyme inhibitor that inhibits the degradation of incretin hormones by DPP-4, and enhances the function of GLP-1 and GIP to increase insulin release and decrease glucagon levels in the circulation in a glucose-dependent manner.

Drug Characteristics: Saxagliptin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 50-75%, food has no effect on absorption
Dose Adjustment Renal	CrCl ≤50 mL/min, 2.5 mg po daily	**Distribution**	Vd = 2.7 L/kg; negligible protein binding
Dialyzable	Yes	**Metabolism**	Hepatic via CYP3A4/5 to metabolite with 50% activity of parent compound; substrate of P-glycoprotein
Pregnancy Category	B	**Elimination**	Renal elimination is 60% with a half-life of 2.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to saxagliptin	**Black Box Warnings**	None

Medication Safety Issues: Saxagliptin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	SitaGLIPtin, SUMAtriptan	No

Drug Interactions: Saxagliptin

Typical Agents	Mechanism	Clinical Management
P-glycoprotein inducers	Increased saxagliptin transport reduces saxagliptin effectiveness	Monitor and consider dose increases of saxagliptin
P-glycoprotein inhibitors	Decreased saxagliptin transport increases risk of saxagliptin toxicity	Monitor and consider dose decreases of saxagliptin
CYP3A4/5 inducers	Increased saxagliptin metabolism reduces saxagliptin effectiveness	Monitor and consider dose increases of saxagliptin
CYP3A4/5 inhibitors	Decreased saxagliptin metabolism increases risk of saxagliptin toxicity	Reduce dose to 2.5 mg daily if concurrent strong CYP3A4/5 inhibitor. Monitor and consider dose decreases of saxagliptin for moderate CYP3A4/5 inhibitor
Corticosteroids (orally inhaled, systemic)	May diminish or increase hypoglycemic effect of saxagliptin	Monitor and consider saxagliptin dose adjustment
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Saxagliptin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypoglycemia	Headaches, nasopharyngitis, peripheral edema, nausea, diarrhea	Pancreatitis, hypersensitivity, acute renal failure, Stevens-Johnson syndrome, rhabdomyolysis

Efficacy Monitoring Parameters. Pre-prandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Monitor renal function and amylase periodically. Seek medical attention if severe skin rash, severe abdominal pain, muscle weakness or pain, or decreased urine production.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times/d). Take with morning meal if once-daily dosing. Take with morning and evening meal if twice-a-day dosing.

Clinical Pearls. Not for use in children. Metformin is first-line therapy for type 2 diabetes. Saxagliptin may be used as monotherapy in a patient with contraindications to metformin. Also available in combination dosage form with metformin. Incretin mimetics may increase risk of pancreatitis and pancreatic duct metaplasia.

SERTRALINE: Zoloft, Various

Class: SSRI Antidepressant

Dosage Forms. Oral Tablet: 25 mg, 50 mg, 100 mg; **Oral Solution, Oral Syrup:** 20 mg/mL

Northstar Rx generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Depression: 50 mg po daily, may titrate to 200 mg/d
2. OCD: Children 6-12 y of age, 25 mg po daily, may titrate to 200 mg/d; Children 13-17 y of age and Adults, 50 mg po daily, may titrate to 200 mg/d
3. Panic disorder, posttraumatic stress disorder, social phobia disorder: 25 mg po daily for 1 wk, then titrate to 50 mg po daily, may titrate to 200 mg/d
4. Premenstrual dysphoric disorder: 50 mg po daily continuously or only during luteal phase; may titrate to 100 mg/d

Off-Label Uses.

1. Binge eating disorder: 25 mg po daily after lunch × 3 d, then titrate to 50 mg po daily, may titrate to 200 mg/d
2. Bulimia nervosa: 50 mg po daily for 1 wk, may titrate to 200 mg/d
3. Generalized anxiety disorder: 25 mg po daily for 1 wk, may titrate to 200 mg/d

MOA. Sertraline is an SSRI that indirectly results in a downregulation of β-adrenergic receptors. It has no clinically important effect on noradrenergic or histamine receptors and no effect on MAO. It lacks stimulant, cardiovascular, anticholinergic, and convulsant effects.

Drug Characteristics: Sertraline

Dose Adjustment Hepatic	Lower dose or dose less frequently	**Absorption**	F = 100%, food has minimal effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 20 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic via CYP2D6 to 1 active metabolite; CYP2D6 substrate; moderate inhibitor of CYP2B6, 2C19, and 2D6
Pregnancy Category	C	**Elimination**	Renal elimination is 40-45% with a half-life of 24 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to sertraline; concomitant use of pimozide, thioridazine, or MAOIs	**Black Box Warnings**	Suicidality, not approved for depression in children; approved for OCD in children >6 y

Medication Safety Issues: Sertraline

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zocor, selegiline	No

Drug Interactions: Sertraline

Typical Agents	Mechanism	Clinical Management
CYP2D6 inhibitors	Decreased sertraline metabolism increases risk of sertraline toxicity	Monitor and consider dose decreases of sertraline
CYP2B6, 2C19, 2D6, substrates	Decreased substrate metabolism may result in substrate toxicity	Monitor and consider decreasing dose of substrate
Antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding
Triptans, SSRIs, dextroampheta-mine, tramadol, MAOIs, linezolid	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome (rest-lessness, hyperthermia, hyper-ref exia, incoordination)

Adverse Reactions: Sertraline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, fatigue, head-ache, insomnia, nausea	Abdominal pain, anxiety, bleeding, constipation, dizziness, diaphoresis, disor-der of ejaculation, indigestion, loss of appetite, rash, reduced libido, somno-lence, sweating, tremor, vomiting, weight gain, xerostomia	Serotonin syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in symptoms of depression, panic disorder, OCD.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding. Monitor CBC.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation; may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

Clinical Pearls. If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Oral concentrate must be diluted before administration. Medication guide required at dispensing.

SILDENAFIL: Viagra, Revatio, Various

Class: Erectile Dysfunction Agent, Pulmonary Hypertension Agent

Dosage Forms. Oral Tablet: 20 mg, 25 mg, 50 mg, 100 mg; **Oral Suspension:** 10 mg/mL

Pfizer pictured

Common FDA Label Indication, Dosing, and Titration.

1. Erectile dysfunction: 25-100 mg po prn 1 h prior to anticipated sexual activity
2. Pulmonary hypertension (WHO group I): 5-20 mg po tid

Off-Label Uses.

1. Pulmonary hypertension (WHO group II-IV): 5-20 mg po tid

MOA. Inhibition of phosphodiesterase type 5 (PDE5) by sildenafil increases the amount of cyclic guanosine monophosphate (GMP) enhancing erectile function and pulmonary vasculature relaxation. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum and vasodilation in the pulmonary bed.

Drug Characteristics: Sildenafil

Dose Adjustment Hepatic	Avoid use in severe liver disease	**Absorption**	F = 41%, food has minimal effect on absorption
Dose Adjustment Renal	CrCl <30 mL/min, 25 mg po if used for ED. Not required for pulmonary artery hypertension (PAH)	**Distribution**	Vd = 105 L; 96% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic via CYP3A4/5
Pregnancy Category	B	**Elimination**	Renal elimination is 13% with a half-life of 4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to phosphodiesterase inhibitors, concurrent nitrates, concurrent HIV protease inhibitors when used for treating pulmonary hypertension	**Black Box Warnings**	None

Medication Safety Issues: Sildenafil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Silodosin, tadalafil	No

Drug Interactions: Sildenafil

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased sildenafil metabolism reduces sildenafil effectiveness	Monitor and consider dose increases of sildenafil
CYP3A4/5 inhibitors	Decreased sildenafil metabolism increases risk of sildenafil toxicity	Reduce dose to 25 mg if concurrent strong CYP3A4/5 inhibitors
α-Adrenergic agents	Additive hypotension	Monitor for hypotension and consider dose reductions
Nitrates	Additive hypotension, potentially severe	Contraindicated
Protease inhibitors	Increased concentration of sildenafil and increased risk of toxicity	Reduce dose of sildenafil to 25 mg every 48 h if used for ED; concurrent use is contraindicated if used for PAH

Adverse Reactions: Sildenafil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Flushing, nausea, headache, visual disturbances, lack of blue/green color discrimination	Nasopharyngitis, angina, chest pain, hypotension, retinal hemorrhage	Myocardial infarction, seizures, strokes, sudden hearing loss, priapism

Efficacy Monitoring Parameters. Improvement in sexual function, improvement in respiratory status/functional status.

Toxicity Monitoring Parameters. Seek medical attention if severe skin rash, chest pain, erection lasting more than 4 h, tinnitus, dizziness, or shortness of breath.

Key Patient Counseling Points. Take 60 min prior to anticipated sexual activity, but do not take more frequently than once q24h.

Clinical Pearls. The choice between tadalafil, sildenafil, or vardenafil is largely one of patient preference; tadalafil would be indicated in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of nitric oxide; the inhibition of PDE5 has no effect in the absence of sexual stimulation. Dose-dependent increase in mortality in children using for PAH; use alternative agent if possible. Revatio is brand name for PAH indication.

SIMVASTATIN: Zocor, Various

Class: HMG-CoA Reductase Inhibitor

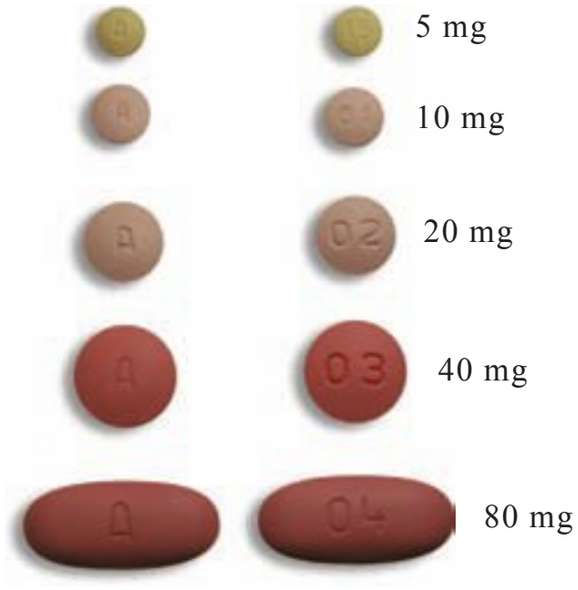
Dosage Forms. Oral Tablet: 5 mg, 10 mg, 20 mg, 40 mg, 80 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hyperlipidemia: 20-40 mg po daily in the evening
2. Primary and secondary preventions of atherosclerotic cardiovascular disease: 20-40 mg po daily in the evening
3. Secondary prevention of cardiovascular events in patients with or at high risk for CAD: 5-40 mg po daily in the evening
4. Familial hypercholesterolemia (homozygous): Children (boys and postmenarchal girls 10-17 y of age), 10 mg po daily, may titrate to 40 mg po daily in the evening; Adults 20-40 mg po daily in the evening

Off-Label Uses. None

MOA. HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol also can decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.



Northstar Rx generic pictured

Drug Characteristics: Simvastatin

Dose Adjustment Hepatic	Contraindicated in active liver disease	**Absorption**	F <5%
Dose Adjustment Renal	Severe renal impairment, initiate at 5 mg po daily	**Distribution**	95% protein bound
Dialyzable	Unknown	**Metabolism**	Extensive hepatic into 3 active metabolites; CYP3A4/5 substrate
Pregnancy Category	X	**Elimination**	Fecal elimination is 60%
Lactation	Contraindicated	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to simvastatin, active liver disease, pregnancy and lactation	**Black Box Warnings**	None

Medication Safety Issues: Simvastatin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zoloft, ZyrTEC atorvaSTATin	No

Drug Interactions: Simvastatin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased simvastatin metabolism reduces simvastatin effectiveness	Monitor and consider dose increases of simvastatin
Moderate CYP3A4/5 inhibitors	Decreased simvastatin metabolism increases risk of simvastatin toxicity	With concurrent amiodarone, amlodipine, lomitapide, or ranolazine, *max* dose of simvastatin is 20 mg daily. With concurrent diltiazem, dronedarone or verapamil, *max* dose of simvastatin is 10 mg daily. Monitor and consider dose decreases of simvastatin if used with other inhibitors
Strong CYP3A4/5 inhibitors	Decreased simvastatin metabolism increases risk of simvastatin toxicity	Concurrent use contraindicated
Fibrates, niacin	Increased risk of myopathy or rhabdomyolysis	Avoid concurrent use, or monitor for myopathy and measure creatine kinase levels
Warfarin	Increased risk of bleeding and risk of rhabdomyolysis	Monitor INR with addition or withdrawal of simvastatin; monitor for myopathy and measure creatine kinase levels

Adverse Reactions: Simvastatin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myalgia, nausea, rash	Rhabdomyolysis, myopathy, hepatotoxicity, tendon rupture, elevated HgA_{1c}, immune-mediated necrotizing myopathy

Efficacy Monitoring Parameters. Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels. Obtain baseline lipid panel, fasting lipid panel 4-12 wk after initiation of therapy and every 3-12 mo thereafter.

Toxicity Monitoring Parameters. Obtain baseline LFTs, SCr, and BUN. Repeat LFTs if signs of hepatotoxicity (fatigue, abdominal pain, yellowing of skin or sclera). Consider CPK in patients with symptoms of myopathy (pain cramping, weakness)

Key Patient Counseling Points. Contact prescriber immediately if pregnancy occurs. Do not drink alcohol. There are multiple significant drug-drug interactions with simvastatin. Consult a health-care professional prior to starting any new medications, including OTC and herbal drugs. Simvastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

Clinical Pearls. May increase fasting blood glucose; however, cardiovascular benefits outweigh the risk of dysglycemia. Myopathy is related to both dose and interacting medications. Simvastatin 80 mg is limited to patients maintained on this dose >12 mo without myopathy or interacting medications. Patients not at LDL goal on 40 mg of simvastatin or requiring high-intensity therapy (eg, LDL >190 mg/dL) should receive alternative therapy.

SITAGLIPTIN: Januvia

Class: Dipeptidyl Peptidase-4 Inhibitor, Antidiabetic

Dosage Forms. Oral Tablet: 25 mg, 50 mg, 100 mg

Common FDA Label Indication, Dosing, and Titration.

1. Diabetes mellitus: 100 mg po daily

Off-Label Uses. None

MOA. Sitagliptin phosphate is a DPP-4 enzyme inhibitor that inhibits the degradation of incretin hormones by DPP-4, and enhances the function of GLP-1 and GIP to increase insulin release and decrease glucagon levels in the circulation in a glucose-dependent manner.

Merck 100 mg pictured

Drug Characteristics: Sitagliptin

Dose Adjustment Hepatic	Not required	**Absorption**	F = 87%, food has no effect on absorption
Dose Adjustment Renal	CrCl 30-50 mL/min, 50 mg po daily; CrCl <30 mL/min, 25 mg po daily	**Distribution**	Vd = 198 L; 38% protein bound
Dialyzable	Yes	**Metabolism**	Substrate of P-glycoprotein; not metabolized
Pregnancy Category	B	**Elimination**	Renal elimination is 87% with a half-life of 12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to sitagliptin	**Black Box Warnings**	None

Medication Safety Issues: Sitagliptin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	SitaGLIPtin	No	Yes	Janumet, saxagliptin	No

Drug Interactions: Sitagliptin

Typical Agents	Mechanism	Clinical Management
P-glycoprotein inducers	Increased sitagliptin transport reduces sitagliptin effectiveness	Monitor and consider dose increases of sitagliptin
P-glycoprotein inhibitors	Decreased sitagliptin transport increases risk of sitagliptin toxicity	Monitor and consider dose decreases of sitagliptin
Corticosteroids	May diminish or increase hypoglycemic effect of sitagliptin	Monitor and consider sitagliptin dose adjustment
MAOIs	Stimulation of insulin secretion, hypoglycemic effects	Avoid concurrent use if possible; monitor and consider dose adjustments

Adverse Reactions: Sitagliptin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypoglycemia	Headaches, nasopharyngitis, nausea, diarrhea	Pancreatitis, hypersensitivity, acute renal failure, Stevens-Johnson syndrome, rhabdomyolysis

Efficacy Monitoring Parameters. Preprandial blood glucose between 70 and 130 mg/dL, HbA_{1c} <7%.

Toxicity Monitoring Parameters. Monitor renal function and amylase periodically. Seek medical attention if severe skin rash, severe abdominal pain, muscle weakness or pain, or decreased urine production.

Key Patient Counseling Points. Monitor blood glucose in frequent intervals (2-4 times/d). Take with morning meal if once-daily dosing. Take with morning and evening meal if twice-a-day dosing. When used in combination with insulin or sulfonylureas, risk of hypoglycemia may be increased.

Clinical Pearls. Not for use in children. Metformin is first-line therapy for type 2 diabetes. Sitagliptin may be used as monotherapy in a patient with contraindications to metformin. Also available in combination dosage form with metformin. Incretin mimetics may increase risk of pancreatitis and pancreatic duct metaplasia. Medication guide must be dispensed with this product.

SOLIFENACIN: Vesicare

Class: Urinary Antispasmodic; Anticholinergic Agent

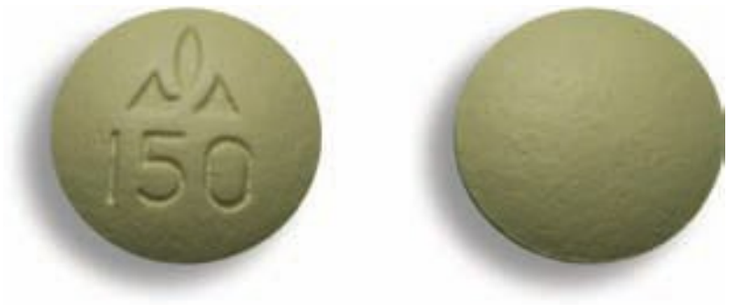
Dosage Forms. Oral Tablet: 5 mg, 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Overactive bladder: 5 mg po daily, may titrate to 10 mg po daily

Off-Label Uses. None

MOA. Solifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.



GlaxoSmithKline 5 mg pictured

Drug Characteristics: Solifenacin

Dose Adjustment Hepatic	Moderate hepatic dysfunction, *max* dose of 5 mg po daily; severe hepatic dysfunction, avoid use	**Absorption**	F = 90%, food has no effect on absorption
Dose Adjustment Renal	CrCl <30 mL/min, *max* 5 mg po daily	**Distribution**	Vd = 600 L; 98% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic; CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 70% with a half-life of 45-68 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to solifenacin, gastric retention, uncontrolled glaucoma, urinary retention	**Black Box Warnings**	None

Medication Safety Issues: Solifenacin

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	VESIcare	Swallow tablet whole	No	Visicol	No

Drug Interactions: Solifenacin

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased solifenacin metabolism reduces solifenacin effectiveness	Monitor and consider dose increases of solifenacin
CYP3A4/5 inhibitors	Decreased solifenacin metabolism increases risk of solifenacin toxicity	Monitor and consider dose decreases of solifenacin
Anticholinergic agents	Additive anticholinergic adverse effects	Avoid concurrent use or monitor carefully for adverse effects
Agents that increase QT interval	Increased risk of QT prolongation (torsades de pointes, cardiac arrest)	Avoid concurrent use or monitor carefully

Adverse Reactions: Solifenacin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, xerostomia, blurred vision	Abdominal pain, dizziness, indigestion, urinary retention	Angioedema, QT prolongation, exfoliative dermatitis

Efficacy Monitoring Parameters. Resolution of clinical signs of incontinence and urinary urgency and frequency.

Toxicity Monitoring Parameters. Seek medical attention for severe anticholinergic effects (severe dry mouth, cognitive impairment, constipation, vision changes). Monitor vital signs.

Key Patient Counseling Points. This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment and/or exercise.

Clinical Pearls. Patients should be advised to exercise caution in driving or other tasks that require alertness until the drug's effects have been determined. May cause decline in cognitive function, especially in the elderly.

SPIRONOLACTONE: Aldactone, Various

Class: Potassium-Sparing Diuretic; Selective Aldosterone Blocker

Dosage Forms. Oral Tablet: 25 mg, 50 mg, 100 mg

25 mg

Amneal generic pictured

50 mg

Actavis generic pictured

100 mg

Amneal generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure, NYHA class III-IV: 12.5-25 mg po daily, may titrate to *max* of 50 mg
2. Edema associated with heart failure: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
3. Nephrotic syndrome: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
4. Hypertension: 50-100 mg po daily in single or divided doses, may titrate to 400 mg/d
5. Hypokalemia: 25-100 mg po daily

Off-Label Uses.

1. Ascites, cirrhosis of liver: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
2. Acne vulgaris: 50-200 mg po daily
3. Hirsutism: 50-200 mg po daily for 20 d/mo

MOA. Spironolactone is a steroidal competitive aldosterone antagonist that acts from the interstitial side of the distal and collecting tubular epithelium to block sodium-potassium exchange, producing a delayed and mild diuresis. The diuretic effect is maximal in states of hyperaldosteronism. Excretion of sodium and chloride excretion is increased; excretion of potassium and magnesium is decreased. Spironolactone has mild antihypertensive activity and has demonstrated a beneficial effect in NYHA class III and IV heart failure.

Drug Characteristics: Spironolactone

Dose Adjustment Hepatic	Alternate-day dosing may be considered	**Absorption**	F = 73%, food increases absorption
Dose Adjustment Renal	CrCl <30 mL/min, not recommended	**Distribution**	90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic to active metabolites
Pregnancy Category	C	**Elimination**	Renal elimination is 47-57% with a half-life of 1.4 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to spironolactone, anuria, acute renal insufficiency, hyperkalemia	**Black Box Warnings**	Tumorigenic in animal models

Medication Safety Issues: Spironolactone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Aldactazide	Avoid >25 mg/d in patients with heart failure or with a CrCl <30 mL/min

Drug Interactions: Spironolactone

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
ACE-Is, angiotensin receptor antagonists	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Eplerenone, potassium supplements, salt substitutes	Increased risk of hyperkalemia	Avoid concurrent use or monitor serum potassium levels
NSAIDs	Decreased antihypertensive effect of spironolactone, increased risk of hyperkalemia	Avoid concurrent use or monitor BP and potassium levels
Digoxin, sotalol	Increased risk of proarrhythmic effects	Monitor ECG and serum potassium and magnesium levels

Adverse Reactions: Spironolactone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Breast tenderness, diarrhea, disorder of menstruation, gastritis, gynecomastia, headache, hyperkalemia, hyponatremia, impotence, lethargy, nausea, rash, stomach cramps, vomiting, urticaria	Cardiac arrhythmias, gastric hemorrhage

Efficacy Monitoring Parameters. Decreased BP, reduction in edema, weight.

Toxicity Monitoring Parameters. Monitor SCr, potassium levels, ECG if symptoms of hyperkalemia occur.

Key Patient Counseling Points. May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Report signs/symptoms of hyperkalemia (muscle weakness, fatigue, bradycardia) and hyponatremia (confusion, dry mouth, thirst, weakness, hypotension, decreased urination). Avoid potassium supplements, foods/salt substitutes that are high in potassium. Avoid alcohol and NSAIDs.

Clinical Pearls. Reduce dose when used in combination with other diuretics. May use loading dose of 2-3 times the daily dose on first day for faster diuresis. Tablets smell like peppermint . . . no kidding.

SUMATRIPTAN: Imitrex, Various

Dr. Reddy's generic 100 mg pictured

Class: Antimigraine Serotonin Receptor Agonist

Dosage Forms. **Oral Tablet:** 25 mg, 50 mg, 100 mg; **Nasal Spray:** 5 mg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Migraine: Oral, 25-100 mg po at onset of migraine, may repeat after 2 h prn; *max* 200 mg/d; Nasal, 5-20 mg in 1 nostril, may repeat after 2 h; *max* 40 mg/d

Off-Label Uses. None

MOA. Sumatriptan binds with high affinity to serotonin (5HT) subtypes 1B, 1D, and 1F receptors. It has no significant affinity or pharmacological activity at adrenergic α_1, α_2, or β; dopaminergic D_1 or D_2; muscarinic; or opioid receptors. Serotonin receptor agonists are believed to be effective in migraine either through vasoconstriction (via activation of 5-HT_1 receptors located on intracranial blood vessels) or through activation of 5-HT_1 receptors on sensory nerve endings in the trigeminal system resulting in the inhibition of proinflammatory neuropeptide release.

Drug Characteristics: Sumatriptan

Dose Adjustment Hepatic	Hepatic dysfunction, *max* single dose 50 mg	**Absorption**	F = 15%, high-fat meal increases F
Dose Adjustment Renal	Not required	**Distribution**	Vd = 2.4 L/kg; 14-21% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic via monoamine oxidase
Pregnancy Category	C	**Elimination**	Renal elimination is 60% with a half-life of 2.5 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to sumatriptan, cerebrovascular syndromes, hemiplegic or basilar migraine, ischemic bowel disease, ischemic heart disease, peripheral vascular disease, severe hepatic impairment, uncontrolled hypertension	**Black Box Warnings**	None

Medication Safety Issues: Sumatriptan

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
STATdose	SUMAtriptan	No	No	ZOLMitriptan, sitaGLIPtin	No

Drug Interactions: Sumatriptan

Typical Agents	Mechanism	Clinical Management
SSRIs	Additive pharmacologic effects resulting in excessive serotonergic stimulation	Avoid concurrent use or monitor carefully for signs of serotonin syndrome
Other 5HT agonists	Additive pharmacologic effect leading to dangerous toxicity	Administration within 24 h of other serotonin agonists is contraindicated
MAOIs	Metabolism of sumatriptan inhibited by MAOI, increasing serotonin levels and risk of serotonin syndrome	Contraindicated
Ergot alkaloids	Enhanced vasoconstricting effects	Contraindicated

Adverse Reactions: Sumatriptan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Nausea, asthenia, dizziness, somnolence	Angina, cardiac dysrhythmia, coronary arteriosclerosis, heart block, hypertension, acute myocardial infarction, aphasia, cerebral ischemia, stroke, dystonia, hemiplegia, neuropathy, transient ischemic attack, oculogyric crisis

Efficacy Monitoring Parameters. Resolution of clinical signs of migraine headache.

Toxicity Monitoring Parameters. Signs of ischemic bowel disease (eg, sudden severe abdominal pain, bloody diarrhea) or peripheral vascular disease, serotonin syndrome (eg, agitation, hallucinations, tachycardia, hyperthermia, labile BP, hyperreflexia, incoordination, diarrhea, nausea, and vomiting), ischemic cardiac syndrome, or hypertensive crisis.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause dizziness or somnolence.

Clinical Pearls. Sumatriptan is also available in formulations for injectable administration, and as an oral dosage form in combination with naproxen. These agents are not for prophylaxis; only for the treatment of acute migraine headache. Several serotonin agonists ("triptans") exist for migraine, administered via a variety of routes (oral, inhaled, and injected). Each differs in onset and duration of action. If one agent is ineffective at *max* dose, recommend changing agents or route. Instruct patients to take a 2nd dose 2 or more h after the 1st, if needed, but no more than 200 mg/d. A transdermal form of sumatriptan was approved in 2013, but is not commercially available as of early 2015.

TACROLIMUS: Prograf, Astragraf XL, Various

Class: Calcineurin Inhibitor

Dosage Forms. **Oral Capsule:** 0.5 mg, 1 mg, 5 mg; **Oral Capsule, Extended Release:** 0.5 mg, 1 mg, 5 mg

Common FDA Label Indication, Dosing, and Titration.

1. Cardiac transplant rejection, prophylaxis: 0.075 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability
2. Liver transplant rejection, prophylaxis: Adults, 0.1-0.15 mg/kg/d po in 2 divided doses, may titrate based on clinical response, serum levels, and tolerability; Children, 0.15-0.2 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability
3. Renal transplant rejection, prophylaxis: Immediate release, 0.2 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability; extended release, 0.1-0.2 mg/kg/d po in 1 dose; may titrate based on serum levels and tolerability; immediate-release to extended-release conversion is 1:1

Off-Label Uses.

1. Lung, small bowel, transplant rejection; prophylaxis, graft-versus-host disease, prevention: Use liver transplant dose above
2. Treatment of graft-versus-host disease in allogeneic stem cell transplant: 0.06 mg/kg po twice daily

MOA. Tacrolimus binds to cyclophilin, which inhibits the antigenic response of helper T lymphocytes, which in turn reduces the production of interleukin-2 and suppresses interferon-γ. Inhibition of the immune response limits inflammation.

Sandoz generic 5 mg pictured

Drug Characteristics: Tacrolimus

Dose Adjustment Hepatic	Use doses at the lower end of the dosing range	**Absorption**	F = 14-32%, food decreases absorption
Dose Adjustment Renal	Use doses at the lower end of the dosing range	**Distribution**	Vd = 5-65 L/kg; 99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; substrate of CYP3A4/5 and P-glycoprotein. P-glycoprotein inhibitor
Pregnancy Category	C	**Elimination**	Renal elimination is <1% with a half-life of 11 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to tacrolimus, concurrent ziprasidone use	**Black Box Warnings**	Risk of infection, risk of malignancies

Medication Safety Issues: Tacrolimus

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Extended release	Yes	Gengraf, PROzac, sirolimus	No

Drug Interactions: Tacrolimus

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased tacrolimus metabolism reduces tacrolimus effectiveness	Monitor and consider dose increases of tacrolimus
CYP3A4/5 inhibitors	Decreased tacrolimus metabolism increases risk of tacrolimus toxicity	Monitor and consider dose decreases of tacrolimus
P-glycoprotein substrates	Decreased substrate transport and increased concentrations of substrates	Monitor and consider dose decreases of substrates
Amiloride, potassium-sparing diuretics	Increased risk of hyperkalemia	Avoid concurrent use
Aminoglycosides, amphotericin, cisplatin, gancyclovir	Increased risk of nephrotoxicity	Avoid concurrent use
Agents that increase QT interval	Increased risk of QT prolongation (torsade de pointes, cardiac arrest)	Ziprasidone contraindicated, others, avoid concurrent use or monitor carefully
Live vaccines	Risk of severe infections	Avoid concurrent use

Adverse Reactions: Tacrolimus

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Chest pain, hypertension, alopecia, diabetes, hyperglycemia, hyperkalemia, hypomagnesemia, hyperlipidemia, constipation, diarrhea, nausea, anemia, leukopenia, thrombocytopenia, infection, arthralgia, dizziness, headache, insomnia, neuropathy, myoclonus, seizure, nephrotoxicity, dyspnea, pleural effusions	Pruritus, elevated LFTs	Cardiomegaly, arrhythmia, Stevens-Johnson syndrome, increased risk of cancer, pancreatitis, acute renal failure

Efficacy Monitoring Parameters. Lack of signs of rejection (elevation in SCr for renal transplant, LFTs for liver transplant). Tacrolimus trough whole blood concentrations (target 5-20 ng/mL).

Toxicity Monitoring Parameters. Monitor electrolytes, FPG, BP and SCr, BUN, lipids, and CBC. Itching or hives, swelling of face, hands, mouth facial or throat, chest tightness, trouble breathing, blistering, peeling, or red skin rash, chest pain, change in urination, unusual bruising or bleeding, severe abdominal pain.

Key Patient Counseling Points. Take on an empty stomach. Avoid alcohol, grapefruit, and grapefruit juice. Many medications, OTC medications, and foods interact with tacrolimus. Monitor carefully.

Clinical Pearls. Tacrolimus is more effective in preventing acute rejection than cyclosporine for patients with liver and kidney transplants. When changing between brand and generic forms, monitor tacrolimus levels. Medication guide required when dispensing this medication. Topical formulation, used for dermatitis, also available.

TADALAFIL: Cialis, Adcirca

Class: Erectile Dysfunction Agent; Pulmonary Hypertension Agent

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg

Common FDA Label Indication, Dosing, and Titration.

1. Erectile dysfunction: Daily use, Cialis only, 2.5-5 mg po daily; PRN use, 10-20 mg po 30 min prior to anticipated sexual activity, *max* frequency is once daily
2. Benign prostatic hyperplasia: Cialis only, 5 mg po daily; when combined with finasteride, tadalafil administration should be discontinued at or before 26 wk.
3. Pulmonary hypertension: Adcirca only, 40 mg po daily

Off-Label Uses. None

Lilly pictured

MOA. Inhibition of phosphodiesterase type 5 (PDE5) by tadalafil enhances erectile function by increasing the amount of cyclic GMP enhancing erectile function and pulmonary vasculature relaxation. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum and vasodilation in the pulmonary bed.

Drug Characteristics: Tadalafil

Dose Adjustment Hepatic	Avoid use	**Absorption**	Well absorbed, food has no effect on absorption
Dose Adjustment Renal	CrCl 31-50 mL/min, *max* dose 10 mg q48h; CrCl <30 mL/min, *max* dose is 5 mg q72h	**Distribution**	Vd = 63-77 L; 94% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal elimination is 36% with a half-life of 15-35 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to phosphodiesterase inhibitors, concurrent nitrates	**Black Box Warnings**	None

Medication Safety Issues: Tadalafil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Sildenafil, vardenafil	No

Drug Interactions: Tadalafil

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased tadalafil metabolism reduces tadalafil effectiveness	Monitor and consider dose increases of tadalafil
CYP3A4/5 inhibitors	Decreased tadalafil metabolism increases risk of tadalafil toxicity	Max dose of 2.5 mg daily dose or 10 mg every 72 h as needed if concurrent strong CYP3A4/5 inhibitors. Monitor and consider dose decreases of tadalafil if concurrent moderate CYP3A4/5 inhibitors
α-adrenergic agents	Additive hypotension	Monitor for hypotension and consider dose reductions
Nitrates	Additive hypotension, potentially severe	Contraindicated

Adverse Reactions: Tadalafil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Flushing, nausea, myalgia, headache	Nasopharyngitis, angina, chest pain, hypotension	Stevens-Johnson syndrome, myocardial infarction, seizures, strokes, sudden hearing loss

Efficacy Monitoring Parameters. Improvement in sexual function, BPH symptoms, or respiratory symptoms.

Toxicity Monitoring Parameters. Seek medical attention if severe skin rash, chest pain, erection lasting >4 h, tinnitus, dizziness, or shortness of breath.

Key Patient Counseling Points. If taking as needed, take 30 min prior to anticipated sexual activity. Do not take more frequently than once q24h. Avoid driving or other activities that require mental alertness until the drug's effects have been determined.

Clinical Pearls. The choice between tadalafil, sildenafil, and vardenafil is largely one of patient preference; tadalafil may be preferred in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of NO; the inhibition of PDE5 has no effect in the absence of sexual stimulation. Adcirca is FDA approved for pulmonary artery hypertension; Cialis is FDA approved for erectile dysfunction.

TAMSULOSIN: Flomax, Various

Boehringer Ingelheim 0.4 mg pictured

Class: α_1-Adrenergic Blocker

Dosage Forms. Oral Capsule: 0.4 mg

Common FDA Label Indication, Dosing, and Titration.

1. Benign prostatic hyperplasia: 0.4 mg po daily, may titrate to 0.8 mg po daily

Off-Label Uses.

1. Neurogenic bladder: 0.4 mg po daily
2. Bladder outlet obstruction symptoms: 0.4 mg po daily
3. Ureteral stones, expulsion: 0.4 mg po daily, discontinue after successful expulsion

MOA. Tamsulosin is closely related to quinazoline derivatives that selectively block postsynaptic α_1-adrenergic receptors. Total peripheral resistance is reduced through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic α_2-receptor blockade. The drugs also decrease total cholesterol, increase HDL-cholesterol, and may improve glucose tolerance and reduce left ventricular mass during long-term therapy. They increase urine flow in BPH by relaxing smooth muscle tone in the bladder neck and prostate.

Drug Characteristics: Tamsulosin

Dose Adjustment Hepatic	Not required	**Absorption**	F >90%, fasting increase F by 30%
Dose Adjustment Renal	Not required	**Distribution**	Vd = 16 L; 94-99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive hepatic; CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	Renal elimination is 10% with a half-life of 9-13 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to tamsulosin	**Black Box Warnings**	None

Medication Safety Issues: Tamsulosin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Yes	No	Flomax, terazosin	No

Drug Interactions: Tamsulosin

Typical Agents	Mechanism	Clinical Management
α_1-Blockers	Increases risk of hypotension	Contraindicated
CYP3A4/5 inducers	Increased tamsulosin metabolism reduces tamsulosin effectiveness	Monitor and consider dose increases of tamsulosin
CYP3A4/5 inhibitors	Decreased tamsulosin metabolism increases risk of tamsulosin toxicity	Avoid strong CYP3A4/5 inhibitors. Monitor and consider dose decreases of tamsulosin with concurrent moderate CYP3A4/5
Beta-blockers, calcium channel blockers, MAOIs	Increased risk of hypotension, especially with 1st dose	Monitor BP

Adverse Reactions: Tamsulosin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, headache, abnormal ejaculation, rhinitis	Asthenia, edema, fatigue, hypotension, nausea, somnolence, vertigo	Retinal detachment, priapism

Efficacy Monitoring Parameters. American Urological Association (AUA) Symptom Score, decrease in residual urine volume, increased urine flow.

Toxicity Monitoring Parameters. Sign/symptoms of hypotension, BP.

Key Patient Counseling Points. Administer 30 min after same meal daily as fasting increases bioavailability by 30%. Patient should avoid activities requiring coordination until drug effects are realized, as drug may cause vertigo or dizziness. Tell patient to rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. Caution patient that syncope or loss of consciousness is possible with first dose or dose increases, especially if patient is in an upright position.

Clinical Pearls. Alpha-blockers commonly used for hypertension. Patients with both hypertension and BPH should avoid taking other α-adrenergic blocking agents while taking this drug.

TEMAZEPAM: Restoril, Various

Class: Benzodiazepine. C-IV

Dosage Forms. Oral Capsule: 7.5 mg, 15 mg, 22.5 mg, 30 mg

Common FDA Label Indication, Dosing, and Titration.

1. Insomnia: 7.5-30 mg po daily hs

Off-Label Uses. None

MOA. Temazepam is a minor metabolite of diazepam. Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

Sandoz generic 15 mg pictured

Mutual Pharmaceutical generic 7.5 mg pictured

Drug Characteristics: Temazepam

Dose Adjustment Hepatic	Not required	**Absorption**	Well absorbed, food has no effect on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.4 L/kg; 96% protein bound
Dialyzable	Unknown	**Metabolism**	Hepatic via multiple CYP pathways; contribution of each CYP is minor
Pregnancy Category	X	**Elimination**	Renal elimination is 80-90% with a half-life of 4-18 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to temazepam or other benzodiazepines, narrow-angle glaucoma, pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Temazepam

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Vistaril, LORazepam	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium

Drug Interactions: Temazepam

Typical Agents	Mechanism	Clinical Management
Alcohol, opioids, and other CNS depressants	Additive CNS and respiratory depression	Avoid if possible and consider dose reductions of both agents
Theophylline	Decreased benzodiazepine effectiveness via inhibition of adenosine receptors	Monitor and consider dose increases for benzodiazepines

Adverse Reactions: Temazepam

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Drowsiness, somnolence, impaired motor coordination	Hypotension, blurred vision, nausea, diarrhea, confusion, headache	Complex behavior, anaphylaxis, worsening of depression, angioedema, drug dependence

Efficacy Monitoring Parameters. Improved ability to fall asleep and sleep through night.

Toxicity Monitoring Parameters. Seek medical attention if severe drowsiness, thoughts of suicide, allergic reaction, or slow or irregular heartbeat. Monitor vital signs.

Key Patient Counseling Points. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol. Take 30 min prior to bedtime. May cause complex behaviors (driving, talking on phone, etc while not fully awake); bed partner should monitor and temazepam should be discontinued.

Clinical Pearls. Not for long-term use (usually 7-10 d only). Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants with caution; may have additive effects. Avoid abrupt discontinuation after chronic use; may cause seizures.

TERAZOSIN: Hytrin, Various

Sandoz generic pictured

Class: α_1-Adrenergic Blocker

Dosage Forms. Oral Capsule: 1 mg, 2 mg, 5 mg, 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Benign prostatic hyperplasia: 1 mg po daily hs, may titrate to 20 mg/d
2. Hypertension: 1 mg po daily hs, may titrate to 20-40 mg/d

Off-Label Uses. None

MOA. Terazosin selectively blocks postsynaptic α_1-adrenergic receptors. Total peripheral resistance is reduced through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic α_2-receptor blockade. Increases urine flow in BPH by relaxing smooth muscle tone in the bladder neck and prostate.

Drug Characteristics: Terazosin

Dose Adjustment Hepatic	Lower doses may be required	**Absorption**	F = 90%, food delays but does not reduce absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 25-30 L; 90-94% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Not metabolized
Pregnancy Category	C	**Elimination**	Renal elimination is 40% with a half-life of 9-12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to terazosin	**Black Box Warnings**	None

Medication Safety Issues: Terazosin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	Avoid use as an antihypertensive. High risk of orthostatic hypotension

Drug Interactions: Terazosin

Typical Agents	Mechanism	Clinical Management
Beta-blockers, calcium channel blockers, PDEIs other alpha-blockers, MAOI	Increased risk of hypotension, especially with first dose	Monitor BP

Adverse Reactions: Terazosin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Asthenia, dizziness	Dyspnea, headache, impotence, nausea, nasal congestion, orthostatic hypotension, palpitations, peripheral edema, priapism, somnolence, syncope	Hepatotoxicity

Efficacy Monitoring Parameters. Decreased BP, improvement in obstructive urinary symptoms.

Toxicity Monitoring Parameters. Sign/symptoms of hypotension, increased HR, LFTs.

Key Patient Counseling Points. Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness and somnolence. Rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. May experience syncope or loss of consciousness with 1st dose. Take drug at bedtime to minimize side effects, especially the 1st dose. Avoid sudden discontinuation of drug, as this may cause rebound hypertension. Avoid alcohol while taking this drug.

Clinical Pearls. JNC 8 guidelines do not recommend the use of terazosin, or other alpha-blockers, for the treatment of hypertension. Clinical use should be restricted to the management of BPH.

TERBINAFINE: Lamisil, Various

Class: Antifungal

Dosage Forms. **Oral Tablet:** 250 mg; **Oral Granules:** 125 mg/packet

Common FDA Label Indication, Dosing, and Titration.

1. Onychomycosis due to dermatophyte: Tablet only, 250 mg po daily × 6 wk for fingernails and × 12 wk for toe nails
2. Tinea capitis: Granules only, Children <25 kg, but ≥4 y of age, 125 mg po daily; Children 25-35 kg, 187.5 mg po daily; Children >35 kg, 250 mg po daily

Northstar Rx generic 250 pictured

Off-Label Uses.

1. Cutaneous sporotrichosis: 500 mg po bid × 2-4 wk after all lesions have healed
2. Lymphocutaneous sporotrichosis: 500 mg po bid × 2-4 wk after all lesions have healed

MOA. Terbinafine is an allylamine antifungal that inhibits biosynthesis of ergosterol, an essential component of fungal cell membrane. This results in fungal cell death primarily due to the increased membrane permeability. Terbinafine has been shown to be active against most clinical infections of *T. mentagrophytes* and *T. rubrum*.

Drug Characteristics: Terbinaf ne

Dose Adjustment Hepatic	Hepatic dysfunction, use not recommended	**Absorption**	F = 40%, administration with food increases AUC by 20%
Dose Adjustment Renal	CrCl <50 mL/min, use not recommended	**Distribution**	Vd = 948 L with 99% protein binding
Dialyzable	Not dialyzable	**Metabolism**	Rapidly and extensively metabolized hepatically, substrate of CYP2C9, CYP1A2, CYP3A4/5, CYP2C8, and CYP2C19, all <10%. Strong CYP2D6 inhibitor
Pregnancy Category	B	**Elimination**	Renal elimination is 70% with a half-life of 22-26 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Use with caution in poor CYP2D6 metabolizers
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Terbinaf ne

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
AT	LamISIL	Do not chew granules	No	LaMICtal, Lomotil	No

Drug Interactions: Terbinaf ne

Typical Agents	Mechanism	Clinical Management
CYP2D6 substrates	Terbinafine is a CYP2D6 inhibitor and can reduce metabolism of substrates, increasing risk of toxicity	Avoid concurrent use or monitor for signs of toxicity and consider substrate dose reductions

Adverse Reactions: Terbinaf ne

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, headache	Rash, fever, increased LFTs	Cutaneous lupus erythematosus, erythema multiforme, Stevens-Johnson syndrome, agranulocytosis, neutropenia, pancytopenia, liver failure, systemic lupus erythematosus

Efficacy Monitoring Parameters. Resolution of infection.

Toxicity Monitoring Parameters. Seek medical attention if severe skin reactions occur; if therapy exceeds 6 wk, CBC, LFTs, are warranted.

Key Patient Counseling Points. Instruct patients to report signs/symptoms of rash, infection, or hepatotoxicity. Symptomatic improvement of nail beds may not be seen for several months. Granules should be sprinkled on a spoonful of pudding or other soft, nonacidic food (eg, mashed potatoes) and swallowed without chewing; do not mix granules with applesauce or other fruit-based foods.

Clinical Pearls. Several topical products containing terbinafine, including both prescription and OTC products, are also available for treatment of skin infections.

TESTOSTERONE: AndroGel, Androderm

Class: Androgen, C-III

Dosage Forms. **Transdermal Patch:** 2 mg/24 h, 4 mg/24 h; **Topical Gel:** 1%; 1.62%, 2%; **Transdermal Cream:** 2%; **Mucoadhesive for Buccal Application:** 30 mg; **Topical Solution:** 30 mg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Hypogonadism: 5 g gel (50 mg active drug) daily to clean, dry, intact skin, may titrate dose to 7.5-10 g daily; one 5 mg patch daily × 24 h, may titrate to 7.5 mg/d

Off-Label Uses. None

MOA. Testosterone is an endogenous androgen. Androgens are responsible for normal growth and development of male sex organs. Testosterone is involved in the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution; laryngeal enlargement; vocal cord thickening; alterations in body musculature; and fat distribution.

Solvay Pharmaceuticals pictured

Drug Characteristics: Testosterone

Dose Adjustment Hepatic	Not required	**Absorption**	Approximately 10% of a topically administered dose is absorbed over 24 h
Dose Adjustment Renal	Not required	**Distribution**	98% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal
Pregnancy Category	X	**Elimination**	Renal elimination is 90% with a half-life of 10-100 min
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to testosterone; men with breast or prostate cancer; women who are pregnant, who may become pregnant, or who are breast-feeding	**Black Box Warnings**	Secondary exposure

Medication Safety Issues: Testosterone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
Pump, MC	No	No	No	T-Gel	Avoid unless indicated for moderate to severe hypogonadism

Drug Interactions: Testosterone

Typical Agents	Mechanism	Clinical Management
Warfarin	Testosterone suppresses clotting factors II, V, VII, and X, and competes with warfarin for plasma protein binding, increasing risk of bleeding	Avoid concurrent use, or increase warfarin monitoring

Adverse Reactions: Testosterone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Benign prostatic hyperplasia, testicular atrophy, PSA increase	Acne, headache, gynecomastia, alopecia, impotence, aggressive behavior, hypertension	Edema, liver carcinoma, prostate cancer, polycythemia, hepatotoxicity, DVTs

Efficacy Monitoring Parameters. Development of secondary gender characteristics (hair growth, masculinization).

Toxicity Monitoring Parameters. Hematocrit levels should be monitored, especially in older men. Instruct patients to report signs and symptoms of unusual bleeding/bruising, rapid weight gain, edema, VTE (leg pain or redness) or liver toxicity (jaundice, dark urine, pale stools).

Key Patient Counseling Points. Gel to be applied to clean, dry, intact skin of the shoulders and upper arms and/or abdomen, but should not be applied to genitals. Gel should be allowed to dry well; swimming and showering should be avoided for 5-6 h after application. Patients should keep application site covered, as direct skin contact can transfer drug to others. Virilization has been reported in children who were secondarily exposed to testosterone gel (coming in contact with bare skin around gel application site). Male patients should report too frequent or persistent erections. Female sexual partners of patients using drug should report male-like changes.

Clinical Pearls. In addition to topical dosage forms (gel and patch), other dosage forms include subcutaneous implants and injectable, which are indicated for delayed puberty, breast cancer, female-to-male gender identity disorder, and others. Avoid other medications containing testosterone, including those purchased without a prescription in health food stores or on the Internet. The patch may contain metal; remove prior to MRIs.

TETANUS TOXOID: Daptacel, Adacel, Boostrix

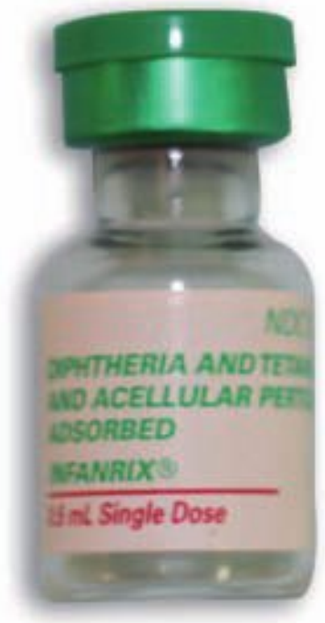
Class: Vaccine, Inactivated, Bacterial

Dosage Forms. Suspension for Intramuscular Injection: Adults and Children ≥7 y of age, available in combination with tetanus and diphtheria toxoids (Td) or combination with tetanus and diphtheria toxoids and acellular pertussis (Tdap); Children ≤6 y of age, available in combination with tetanus and diphtheria toxoids and acellular pertussis (DTaP), and in combination with other pediatric vaccines.

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of tetanus: Children, all infants at 2, 4, 6, and 12-15 mo of age, and a 5th dose at 4-6 y of age, as primary series of DTaP; Tdap at 11-12 y of age; single dose of Tdap for all adults at next opportunity; Td every 10 y for adults

Off-Label Uses. None



Infanrix, GlaxoSmithKline pictured

Drug Characteristics: Tetanus Toxoid

Pregnancy Category	C	**ADME**	None known
Lactation	Caution advised; weigh risk and benefit	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to tetanus toxoid or a component of the vaccine (gelatin, latex, thimerosal)	**Black Box Warnings**	None

Medication Safety Issues: Tetanus Toxoid

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Adacel, Daptacel, Tdap, DTaP	No

Drug Interactions: Tetanus Toxoid

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression, reduced efficacy of vaccine	Delay tetanus toxoid administration until corticosteroid therapy has been discontinued if possible; clinical judgment
Immunosuppressing agents	Immunosuppression, reduced efficacy of vaccine	Delay tetanus toxoid administration until immunosuppressive therapy has been discontinued if possible

Adverse Reactions: Tetanus Toxoid

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb	GI symptoms	Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of tetanus, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

Toxicity Monitoring Parameters. Monitor for syncope, fever after administration.

Key Patient Counseling Points. Return to provider for each dose in the series.

Clinical Pearls. Use the same brand of vaccine to complete the entire series, if possible. After childhood immunization, adults should substitute a 1 time dose of Tdap for Td booster then boost with Td (tetanus with diphtheria) vaccination every 10 y. Pregnant women should receive 1 dose of Tdap vaccine during each pregnancy, preferred during 27-36 wk gestation regardless of interval of last Td or Tdap vaccine. Individuals with wounds requiring medical attention should be vaccinated with Td if vaccination status is inadequate or unknown, or if >5 y since last vaccination.

THYROID: Armour Thyroid, Various

Forest Laboratories pictured

Class: Thyroid Supplement

Dosage Forms. Oral Tablet: 15 mg, 16.25 mg, 30 mg, 32.4 mg, 32.5 mg, 48.75 mg, 60 mg, 64.8 mg, 65 mg, 81.25 mg, 90 mg, 97.5 mg, 113.75 mg, 120 mg, 130 mg, 146.25 mg, 162.5 mg, 180 mg, 195 mg, 240 mg, 260 mg, 300 mg, 325 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypothyroidism: Dosing individualized based on clinical response and serum TSH levels; Infants birth to 6 mo of age, 4.8-6.8 mg/kg/d po daily; Infants 6-12 mo of age, 3.6-4.8 mg/kg/d po daily; Children 1-5 y of age, 3-3.6 mg/kg/d po daily; Children 6-12 y of age, 2.4-3 mg/kg/d po daily; Children >12 y of age, 1.2-1.8 mg/kg/d po daily; Adults, 15-120 mg po daily

Off-Label Uses. None

MOA. Thyroid hormone is a naturally derived thyroid replacement containing both levothyroxine (T_4) and liothyronine (T_3). The endogenous thyroid hormones, T_3 and T_4, diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins.

Drug Characteristics: Thyroid

Dose Adjustment Hepatic	Not required	**Absorption**	F = 48-79%, increases with fasting
Dose Adjustment Renal	Not required	**Distribution**	99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Approximately 80% of levothyroxine sodium is deiodinated into T_3 in the liver, kidney, and other tissues; it can also be metabolized by conjugation with glucuronides and sulfates and then enter into enterohepatic recirculation
Pregnancy Category	A	**Elimination**	Renal excretion is 50% with a half-life of 7 d
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to thyroid, nontoxic diffuse goiter or nodular thyroid disease, thyrotoxicosis, acute MI, treatment of obesity or weight loss, uncorrected adrenal insufficiency; may precipitate acute adrenal crisis	**Black Box Warnings**	Ineffective and potentially toxic when used for weight loss

Medication Safety Issues: Thyroid

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
NP, P	No	No	No	No	Avoid. Concerns about cardiac effects

Drug Interactions: Thyroid

Typical Agents	Mechanism	Clinical Management
Warfarin	Increased risk of bleeding	Monitor INR and consider warfarin does adjustments

Adverse Reactions: Thyroid

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
		Aggravation of preexisting cardiovascular disease, hyperthyroidism

Efficacy Monitoring Parameters. Serum TSH, T_3, and T_4 levels: resolution of symptoms of hypothyroidism, fatigue, edema, hair loss, cold intolerance, lethargy.

Toxicity Monitoring Parameters. Monitor patients with preexisting cardiovascular disease for exacerbation of symptoms.

Key Patient Counseling Points. You may have to take this medicine for 6-8 wk before your symptoms improve. Do not stop using this medicine suddenly without asking your doctor. You may need to slowly decrease your dose before stopping it completely. Take on an empty stomach, with water.

Clinical Pearls. T_3 normal range is 100-200 ng/dL. T_4 normal range is 4.5-11.2 mcg/dL. TSH level should be between 0.5 and 3.0 mIU/L in those successfully treated for a thyroid disorder. When used for weight loss, high doses may cause life-threatening adverse effects.

TIOTROPIUM: Spiriva

Class: Anticholinergic Bronchodilator

Dosage Forms. Inhalation Capsule: 18 mcg

Common FDA Label Indication, Dosing, and Titration.

1. COPD: Inhale contents of 1 capsule (18 mcg) daily using manufacturer-provided device (do not swallow capsules)

Off-Label Uses. None

MOA. Tiotropium is a long-acting antimuscarinic agent, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors, M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3-receptors at the smooth muscle leading to bronchodilation. The bronchodilation following inhalation of tiotropium is predominantly a site-specific effect.

Pfizer/Boehringer Ingelheim pictured

Drug Characteristics: Tiotropium

Dose Adjustment Hepatic	Not required	**Absorption**	After inhalation, well absorbed into the lung; <19.5% of dose is absorbed systemically
Dose Adjustment Renal	Not required	**Distribution**	Vd = 32 L/kg; 72% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal
Pregnancy Category	C	**Elimination**	Renal elimination is 14% (unchanged) with a half-life of 5-6 d
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to tiotropium, ipratropium, or milk protein	**Black Box Warnings**	None

Medication Safety Issues: Tiotropium

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Capsules for inhalation, not oral use	No	Inspra, Serevent	No

Drug Interactions: Tiotropium

Typical Agents	Mechanism	Clinical Management
Other anticholinergic agents	Additive effect with tiotropium	Avoid concurrent use

Adverse Reactions: Tiotropium

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Xerostomia, upper respiratory infection	Constipation, pharyngitis, sinusitis, headache, dysphonia, application site irritation	Bowel obstruction, cerebrovascular accident; bronchospasm

Efficacy Monitoring Parameters. Monitor pulmonary function tests, shortness of breath.

Toxicity Monitoring Parameters. Seek medical attention if severe anticholinergic side effects occur, including bladder obstruction, narrow angle glaucoma, prostatic hyperplasia, and urinary retention or difficulty.

Key Patient Counseling Points. Advise patients that this drug is not indicated for acute bronchospasm (rescue therapy). This drug may cause increased HR, dry mouth, constipation, urinary difficulty and retention, respiratory tract infection, and sinusitis. Warn patients that the drug capsules are for inhalation only and are not to be swallowed; instruct patients on the use of the inhalation device.

Clinical Pearls. Paradoxical bronchospasm has occurred with tiotropium; when it occurs, therapy should be permanently discontinued.

TIZANIDINE: Zanaflex, Various

Class: Centrally Acting Skeletal Muscle Relaxant, α_2-Agonist

Dosage Forms. **Oral Capsule:** 2 mg, 4 mg, 6 mg; **Oral Tablet:** 2 mg, 4 mg

Common FDA Label Indication, Dosing, and Titration.

1. Muscle Spasticity: 2 mg po up to tid, may titrate to 8 mg po q6-8h with *max* dose of 36 mg/d

Off-Label Uses.

1. Acute low back pain: 12 mg/d po alone or in combination with NSAIDs

MOA. Tizanidine is a centrally acting muscle relaxant. The drug is an imidazole derivative, structurally unrelated to other muscle relaxants. Tizanidine is an agonist of α_2-adrenergic receptors, which decreases spasticity by increasing presynaptic inhibition; however, it does not have antihypertensive properties.

Sandoz generic pictured

Drug Characteristics: Tizanidine

Dose Adjustment Hepatic	Use not recommended	**Absorption**	F = 40%, extensive first-pass metabolism; food increases extent of absorption of tablets by 30% but decreases extent of absorption of capsules by 10%
Dose Adjustment Renal	CrCl <25 mL/min, reduce dose	**Distribution**	Vd = 2.4 L/kg; 30% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Extensive (95%) hepatic metabolism to inactive metabolites, substrate of CYP1A2
Pregnancy Category	C	**Elimination**	Renal elimination is 60% with a half-life of 2 h
Lactation	Avoid	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to tizanidine; coadministration with CYP1A2 inhibitors	**Black Box Warnings**	None

Medication Safety Issues: Tizanidine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	TiZANidine	No	No	tiaGABine	No

Drug Interactions: Tizanidine

Typical Agents	Mechanism	Clinical Management
CYP1A2 inhibitors	Inhibition of tizanidine metabolism and increased toxicity	Do not coadminister; select alternative antispasmodic
Phenytoin, fosphenytoin	Unknown mechanism; results in increased serum concentrations of phenytoin and resulting phenytoin toxicity	Monitor for signs of phenytoin toxicity and adjust dose accordingly
CNS depressants	Additive CNS depression	Avoid concurrent use

Adverse Reactions: Tizanidine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Mild hypotension, xerostomia, asthenia, dizziness, somnolence, muscle weakness	Constipation, vomiting, dyskinesia, amblyopia, feeling nervous, syncope, depression	Myocardial infarction, thrombocytopenia, hepatitis, pulmonary embolism, hypersensitivity, death

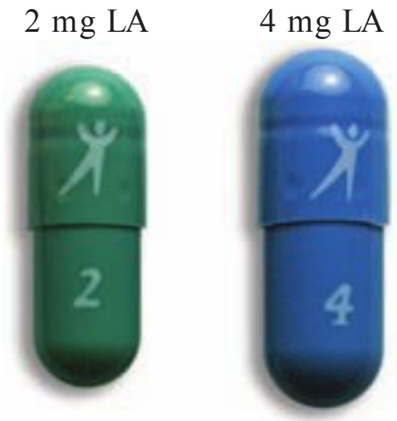
Efficacy Monitoring Parameters. Reduction in pain and muscle spasms, reduction in passive limb movement.

Toxicity Monitoring Parameters. Monitor BP, LFTs, SCr, CBC.

Key Patient Counseling Points. Be cautious of risk of dizziness and somnolence when initiating therapy; do not drive until effects of drug are known. Rise slowly from a lying/sitting position, as this drug may cause hypotension. May cause xerostomia (dry mouth) and asthenia (weakness).

Clinical Pearls. While this drug may be taken with or without food, patients should take the drug in the same way (fasting or fed) every time to avoid inconsistent absorption patterns and resulting changes in efficacy and adverse effects. Effect of food on extent of absorption differs for tablets and capsules. Abrupt discontinuation can cause rebound hypertension and tachycardia. Taper if used at high dose (20-28 mg daily) or for an extended period of time.

TOLTERODINE: Detrol, Detrol LA



Pfizer pictured

Class: Antimuscarinic

Dosage Forms. Oral Tablet: 1 mg, 2 mg; **Oral Capsule, Extended Release:** 2 mg, 4 mg

Common FDA Label Indication, Dosing, and Titration.

1. Bladder muscle dysfunction, overactive: Immediate release, 1-2 mg po bid; Extended release, 2-4 mg po daily; may titrate dose to tolerability and response

Off-Label Uses. None

MOA. Tolterodine, a competitive muscarinic receptor antagonist, has a high binding affinity for the cholinergic muscarinic receptors that mediates contraction of the urinary bladder and decreases salivation. The drug exerts its significant effects on the lower urinary tract by increasing the residual urine and decreasing detrusor pressure.

Drug Characteristics: Tolterodine

Dose Adjustment Hepatic	Hepatic dysfunction, limit dose to 2 mg po daily	**Absorption**	F = 77%; no effect of food on absorption
Dose Adjustment Renal	CrCl 10-30 mL/min, limit dose to 2 mg po daily	**Distribution**	Vd = 113 L; >90% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP2D6 and CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 77% (10% unchanged) and 17% in feces (20% unchanged), with a half-life of 1.9-3.7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Consider lower dose in CYP2D6 poor metabolizers
Contraindications	Hypersensitivity to tolterodine, gastric retention, uncontrolled narrow-angle glaucoma, urinary retention	**Black Box Warnings**	None

Medication Safety Issues: Tolterodine

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
LA	No	Do not chew or crush LA formulation	No	Fesoterodine	No

Drug Interactions: Tolterodine

Typical Agents	Mechanism	Clinical Management
Amiodarone, propafenone, quinidine	Increased QT interval prolongation	Avoid concurrent use
CYP3A4/5 and CYP2D6 inhibitors	Decreased tolterodine metabolism increases risk of toxicity	Reduce dose to 2 mg po daily
CYP3A4/5 inducers	Increased tolterodine metabolism reduces tolterodine effectiveness	Monitor for efficacy and consider dose increases
Warfarin	Increased risk of bleeding	Monitor INR

Adverse Reactions: Tolterodine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Xerostomia	Constipation, dizziness, headache, increased HR, indigestion, somnolence, vertigo, chest pain	Tachycardia, QT prolongation, angioedema, hallucinations

Efficacy Monitoring Parameters. Subjective improvement of urge incontinence (reduced desire to urinate), and urinary frequency.

Toxicity Monitoring Parameters. Assess renal and hepatic function at baseline; monitor vital signs.

Key Patient Counseling Points. Patients should avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause blurred vision, dizziness, and drowsiness. Swallow extended-release capsule whole; do not crush, break, or chew. In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). If symptoms occur, the drug should be discontinued and supportive measures instituted.

Clinical Pearls. May note decline in cognitive function, particularly in elderly. Lifestyle changes can also improve urinary symptoms. Patients should lose weight and avoid beverages containing alcohol or caffeine. Long-acting product is generally better tolerated.

TOLVAPTAN: Samsca

Class: Vasopressin Antagonist

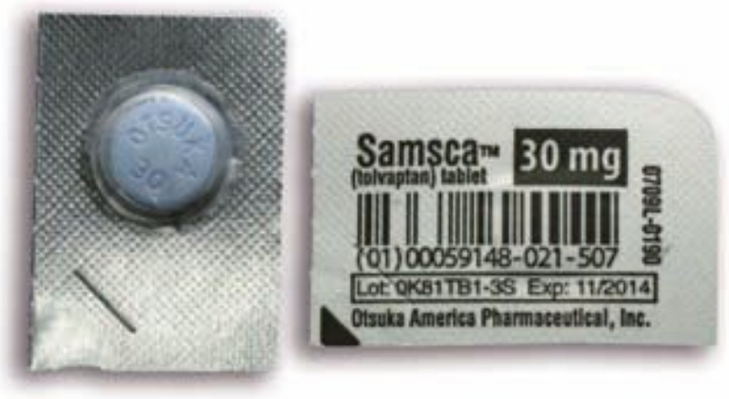
Dosage Forms. Oral Tablet: 15 mg, 30 mg

Common FDA Label Indication, Dosing, and Titration.

1. Hypervolemic or euvolemic hyponatremia: 15 mg po daily, may titrate to *max* of 60 mg po daily

Off-Label Uses. None

MOA. Tolvaptan is a selective vasopressin V_2-receptor antagonist with an affinity for the V_2-receptor that is 1.8 times that of native arginine vasopressin (AVP). When taken orally, tolvaptan antagonizes the effect of vasopressin and causes an increase in urine water excretion that results in an increase in free water clearance, a decrease in urine osmolality, resulting in the restoration of normal serum sodium levels.



Otsuka 30 mg pictured

Drug Characteristics: Tolvaptan

Dose Adjustment Hepatic	Avoid in liver disease	**Absorption**	F = 40%
Dose Adjustment Renal	Avoid use if CrCl <10 mL/min	**Distribution**	Vd = 3 L/Kg; 99% protein bound
Dialyzable	Not known	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Nonrenal routes with half-life of 2.8-12 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Anuria, concurrent use of strong CYP3A4/5 inhibitors, hypovolemic hyponatremia	**Black Box Warnings**	Initiate in hospital to monitor serum sodium. Too rapid correction (eg, >12 mEq/24 h) can results in seizures, coma and death; correct sodium gradually

Medication Safety Issues: Tolvaptan

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Tolvaptan

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased tolvaptan metabolism reduces tolvaptan effectiveness	Monitor and consider dose increases of tolvaptan
CYP3A4/5 inhibitors	Decreased tolvaptan metabolism increases risk of tolvaptan toxicity	Concurrent strong CYP3A4/5 inhibitors is contraindicated, monitor and consider dose decreases of tolvaptan if concurrent moderate CYP3A4/5 inhibitors

Adverse Reactions: Tolvaptan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Increased thirst, nausea, xerostomia, polyuria	Hyperglycemia, constipation, dizziness, dehydration	Hypovolemia, hepatic failure, osmotic demyelination syndrome

Efficacy Monitoring Parameters. Monitor serum sodium levels carefully; normalization of serum sodium is the efficacy parameter.

Toxicity Monitoring Parameters. Monitor for dehydration, serum electrolytes, neurologic status, signs and symptoms of syndrome of inappropriate antidiuretic hormone secretion. Monitor LFTs and discontinue if increased.

Key Patient Counseling Points. May be taken with or without food. Avoid fluid restriction for the first 24 h of therapy. Resume fluid restriction on discontinuation.

Clinical Pearls. Initiate and reinitiate therapy only in the hospital setting, monitoring serum sodium carefully. Should not be used for >30 d in patients with underlying liver disease.

TOPIRAMATE: Topamax, Various

Class: Anticonvulsant

Dosage Forms. **Oral Capsule, Sprinkle:** 15 mg, 25 mg; **Oral Tablet:** 25 mg, 50 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 H**: 25 mg, 50 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 H Sprinkle:** 25 mg, 50 mg, 100 mg, 150 mg, 200 mg

Forest Laboratories generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Partial or tonic-clonic seizure, monotherapy or adjunct: Children 2-16 y of age, 1-3 mg/kg/d (*max* 25 mg) po daily × 1 wk, may titrate to 5-9 mg/kg/d; Children ≥17 y of age and Adults, 25 mg po bid × 1 wk, may titrate to *max* of 200 mg po bid
2. Migraine prophylaxis: Immediate release only, initial 25 mg po daily × 1 wk, may titrate to *max* of 50 mg po bid

Off-Label Uses.

1. Cluster headache prophylaxis: 25 mg po daily, may titrate to *max* of 200 mg/d

MOA. The exact mechanisms by which topiramate exerts its anticonvulsant and migraine prophylaxis effects are unknown. Electrophysiological and biochemical evidence suggests that topiramate blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-aminobutyrate at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV.

Drug Characteristics: Topiramate

Dose Adjustment Hepatic	Hepatic disease, adjust dose and monitor carefully for adverse effects	**Absorption**	F = 80%, no effect of food on absorption
Dose Adjustment Renal	CrCl <70 mL/min, reduce initial and incremental dose adjustments by 50%	**Distribution**	Vd = 0.6-0.8 L/kg; 15-41% protein bound
Dialyzable	Yes	**Metabolism**	Minor
Pregnancy Category	D	**Elimination**	Renal elimination is 70% unchanged with a half-life of 21 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, alcohol use for the ER formulation (within 6 h prior to and 6 h after administration)	**Black Box Warnings**	None

Medication Safety Issues: Topiramate

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	No	Qudexy XR may be opened and sprinkled on food. Do not open Trokendi XR capsule.	No	Sporanox, Toprol XL	No

Drug Interactions: Topiramate

Typical Agents	Mechanism	Clinical Management
Amitriptyline	Concomitant use of amitriptyline and topiramate may increase plasma concentrations of amitriptyline; mechanism unknown	Avoid concurrent use or adjust amitriptyline dose as necessary to avoid amitriptyline toxicity
Oral contraceptives	When used concurrently with estrogen-progestin combination contraceptives, AUC of the estrogenic component is decreased, reducing contraceptive efficacy	Avoid concurrent use or use an alternative nonhormonal contraceptive method of birth control

Adverse Reactions: Topiramate

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Ataxia, loss of appetite, nausea dizziness, impaired psychomotor performance, somnolence, fatigue, nystagmus, low serum bicarbonate	Disorder of language, diplopia, weight loss, depression, nausea, nephrolithiasis	Erythema multiforme, Stevens-Johnson syndrome, hypohidrosis, increased body temperature, metabolic acidosis, liver failure, glaucoma, myopia, suicidal ideation

Efficacy Monitoring Parameters. Decreased seizure frequency or frequency of migraine headaches.

Toxicity Monitoring Parameters. Monitor electrolytes, SCr, hydration, and occurrence of suicidal thoughts.

Key Patient Counseling Points. Avoid activities requiring mental alertness and coordination until drug effects are realized. Drug may cause dizziness and somnolence, especially if taken with alcohol or other CNS depressants. May cause nausea, diplopia, nervousness, confusion, and many other CNS effects. Do not discontinue drug abruptly, as this may cause increased seizure activity. Seek medical attention for new eye problems or high body temperature. May decrease sweating; avoid hot temperatures (including hot tubs and saunas).

Clinical Pearls. When adjusting dose, make small changes slowly ("start low and go slow") to avoid acute adverse effects.

TRAMADOL: Ultram, Various

Class: Opioid Analgesic. C-IV

Dosage Forms. **Oral Tablet:** 50 mg; **Oral Tablet, Extended Release:** 100 mg, 200 mg, 300 mg; **Oral Capsule, Extended Release:** 100 mg (composed of 25 mg immediate release followed by 75 mg extended release), 200 mg (composed of 50 mg immediate release followed by 150 mg extended release), 300 mg (composed of 50 mg immediate release followed by 250 mg extended release); **Oral Suspension:** 10 mg/mL; **Topical Cream:** 5%, 8%

Amneal generic 50 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Pain, chronic, moderate to moderately severe: Immediate release, 50 mg po prn, may titrate to 200 mg/d; extended release, initial, 100 mg po daily, may titrate to 300 mg/d; to convert from immediate release, convert 1:1 and round down to nearest 100 mg dose

Off-Label Uses. None

MOA. Tramadol is a mu agonist and a weak inhibitor of serotonin and norepinephrine reuptake. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation.

Drug Characteristics: Tramadol

Dose Adjustment Hepatic	Moderate or severe, immediate release, 50 mg po q12h; avoid extended-release formulation	**Absorption**	Immediate release: F = 75%, no food effect. Extended release: F = 70%, variable food effect
Dose Adjustment Renal	CrCl <30 mL/min, immediate release, extend interval to q12h (*max* dose of 200 mg po daily); avoid extended-release formulation	**Distribution**	Vd = 3 L; 20% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic, CYP3A4/5 and CYP2D6 substrate
Pregnancy Category	C	**Elimination**	Renal elimination of 30%, with a half-life of 6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	CYP2D6 poor metabolizers have higher concentrations of parent compound and may require lower doses
Contraindications	Hypersensitivity to tramadol or other opioids, paralytic ileus, respiratory depression, bronchial asthma	**Black Box Warnings**	None

Medication Safety Issues: Tramadol

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
ODT	TraMADol	Do not chew or crush ER	No	Tapentadol, Toradol, Trandate, traZODone, Voltaren	No

Drug Interactions: Tramadol

Typical Agents	Mechanism	Clinical Management
Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines	Additive CNS depression	Monitor and consider dose adjustments
Buprenorphine, opioid agonists/antagonists, opioid antagonists	Precipitation of withdrawal symptoms	Avoid concurrent use with opioids
CYP3A4/5 inducers	Increased tramadol metabolism reduces tramadol efficacy	Consider dose increases of tramadol
CYP3A4/5 or CYP2D6 inhibitors	Decreased tramadol metabolism increases risk of tramadol toxicity	Consider dose decreases of tramadol
MAOIs	Additive respiratory depression, increased risk of serotonin syndrome	Contraindicated

Adverse Reactions: Tramadol

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Constipation, GI distress, dizziness, sedation, edema, sweating, pruritus, headaches, flushing	Dyspnea, xerostomia, depression, orthostatic hypotension	Cardiac arrest, physical dependence, tolerance, seizures, pancreatitis, suicidal ideation, anemia

Efficacy Monitoring Parameters. Relief of pain.

Toxicity Monitoring Parameters. Excessive drowsiness; decreased breathing, severe constipation, chest pain, dizziness, signs of tolerance. Monitor vital signs.

Key Patient Counseling Points. Use a stool softener and stimulant or laxative for preventing constipation if used chronically. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

Extended-release products must not be crushed or chewed, but may be taken with or without food, and always the same way to avoid variability in absorption.

Clinical Pearls. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Tramadol-related deaths have been reported in patients with histories of emotional disturbances; suicidal ideation/attempts; or tranquilizer, alcohol, and other CNS-active drug misuse. Suspension and creams are available in compounding kits.

TRAVOPROST: Travatan Z

Class: Prostaglandin, Antiglaucoma Agent

Dosage Forms. Ophthalmic Solution: 0.004%

Common FDA Label Indication, Dosing, and Titration.

1. Ocular hypertension: 1 drop in affected eyes daily in the evening
2. Open-angle glaucoma: 1 drop in affected eyes daily in the evening

Off-Label Uses. None

MOA. Travoprost is a prostaglandin F2-alpha analogue. It is believed to reduce intraocular pressure by increasing the outflow of aqueous humor. Studies suggest that the main mechanism of action is increased uveoscleral outflow, but the exact mechanism is unknown.

Alcon 0.004% solution pictured

Drug Characteristics: Travoprost

Dose Adjustment Hepatic	Not required	**Absorption**	Travoprost is absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active; systemic absorption following ocular instillation is very low
Dose Adjustment Renal	Not required	**Distribution**	Unknown
Dialyzable	Not dialyzable	**Metabolism**	Metabolized within the cornea; any entering systemic circulation is metabolized in the liver, extent unknown
Pregnancy Category	C	**Elimination**	Extent of renal elimination unknown, but half-life of 45 min
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Travoprost

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Xalatan	No

Drug Interactions: Travoprost. None known

Adverse Reactions: Travoprost

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Blurred vision, hyperpigmentation of eyelid, iris pigmentation	Blepharitis, pain in eye, reduced visual acuity, foreign-body sensation	Cataract

Efficacy Monitoring Parameters. Reduction in IOP.

Toxicity Monitoring Parameters. Seek medical attention if symptoms of ocular irritation are severe.

Key Patient Counseling Points. Wash your hands and remove contact lenses before using the medicine. For administration, lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Put the cap on the bottle right away. Do not exceed once-daily dosing (may decrease efficacy). Separate administration of other ophthalmic agents by at least 5 min.

Clinical Pearls. Advise patients that there is a risk of permanent increased iris pigmentation associated with instillation of this product. May change length and number of eye lashes.

TRAZODONE: Desyrel, Oleptro, Various

Class: Antidepressant

Dosage Forms. **Oral Tablet:** 50 mg, 100 mg, 150 mg, 300 mg; **Oral Tablet, Extended Release:** 150 mg, 300 mg

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Immediate release, 150 mg po daily in divided doses, may titrate to 400 mg/d; extended release, 150 mg po daily hs, may titrate to 375 mg/d

Off-Label Uses.

1. Insomnia: Adults, 50 po daily hs

MOA. The mechanism of antidepressant action is not fully understood, but suspected to be related to its potentiation of serotonergic activity in the CNS by inhibiting reuptake of serotonin. Trazodone also significantly blocks histamine (H_1) and α_1-adrenergic receptors.

Teva generic pictured

Mylan generic pictured

Drug Characteristics: Trazodone

Dose Adjustment Hepatic	Hepatic dysfunction, initial dose 25 mg po daily	**Absorption**	F = 65%; food increases absorption
Dose Adjustment Renal	Not required	**Distribution**	89-95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic; CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 70-75% and 21% in feces, with a half-life of 7-10 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, use of MAOI	**Black Box Warnings**	Suicidal ideation, not for use in children

Medication Safety Issues: Trazodone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	TraZODone	Do not crush or chew ER formulation	No	traMADol, ziprasidone	No

Drug Interactions: Trazodone

Typical Agents	Mechanism	Clinical Management
Amiodarone, agents that prolong QT interval	Increased risk of QT prolongation and torsades de pointes	Avoid concomitant use
CYP3A4/5 inhibitors	Decreased trazodone metabolism increases risk of trazodone toxicity	Consider lower trazodone dose; monitor for adverse effects
CYP3A4/5 inducers	Increased trazodone metabolism reduces trazodone efficacy	Monitor trazodone levels
Digoxin	Increased digoxin concentrations and risk of toxicity	Monitor digoxin levels
Fluoxetine, linezolid, paroxetine, venlafaxine	Increased risk of trazodone side effects or serotonin syndrome	Monitor for adverse effects

Adverse Reactions: Trazodone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, sedation, headache, nausea, somnolence, xerostomia	Backache, blurred vision, constipation, diarrhea, fatigue, feeling nervous, headache, hypotension, insomnia, syncope, tremor, vomiting	Bleeding risk, cardiac dysrhythmia, fractures, priapism, prolonged QT, serotonin syndrome, suicidal thoughts, torsade de pointes

Efficacy Monitoring Parameters. Improvement in depressive symptoms (depressed mood, suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, lack of pleasure/interest in usual activities, feeling of excessive guilt/worthlessness, psychomotor retardation or agitation, difficulties in thinking/concentration/memory).

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Irregular HR in patients with cardiac disease and/or risk factors associated with QT prolongation. Signs/symptoms of peripheral edema, increased HR, signs/symptoms of liver damage. Monitor ECG, LFT, SCr, BUN, and vital signs.

Key Patient Counseling Points. Extended-release tablet may be broken in half, but do not chew or crush. Extended-release tablets should be taken on an empty stomach, but the immediate-release tablets should be taken with food. Patients should avoid driving and other activities requiring mental alertness or coordination until drug effects are realized, as this medicine may cause dizziness or somnolence. Report signs/symptoms of priapism immediately. Report use of MAOI within the past 14 d. Advise patients against sudden discontinuation of drug. Do not drink alcohol, or use barbiturates or other CNS depressants while taking this drug.

Clinical Pearls. Antidepressants increased the risk of suicidal thinking and behavior in children, adolescents, and young adults in short-term studies with major depressive disorder (MDD) and other psychiatric disorders. This risk must be balanced with the clinical need. Monitor patients closely for clinical worsening, suicidality, or unusual changes in behavior.

TRIAMCINOLONE NASAL: Nasacort AQ

Class: Intranasal Adrenal Glucocorticosteroid

Dosage Forms. Nasal Spray: 55 mcg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Perennial or seasonal allergic rhinitis: Children 2-5 y of age, 1 spray/nostril daily, *max* of 110 mcg/d; Children 6-12 y of age, 1 spray/nostril daily, *max* of 220 mcg/d; Children >12 y of age and Adults, initial, 2 spray/nostril daily, *max* of 220 mcg/d; maintenance, 1 spray/nostril daily, *max* of 110 mcg/d

Off-Label Uses. None

MOA. Triamcinolone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins, resulting in suppression of the immune system. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid.

Sanofi-Aventis pictured

Drug Characteristics: Triamcinolone Nasal

Dose Adjustment Hepatic	Not required	**Absorption**	<2% of dose absorbed systemically after nasal administration
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Triamcinolone Nasal

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	NasalCrom, do not use TAC as an abbreviation for triamcinolone	No

Drug Interactions: Triamcinolone Nasal. None known

Adverse Reactions: Triamcinolone Nasal

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Nasal irritation and burning, headache, pharyngitis	Epistaxis, taste perversion	Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis

Efficacy Monitoring Parameters. Control of rhinitis signs and symptoms.

Toxicity Monitoring Parameters. While only small amounts of triamcinolone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression and infection.

Key Patient Counseling Points. Advise patients on the proper administration technique for this product. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

Clinical Pearls. Injectable, oral inhalation, and topical dosage forms of triamcinolone also available for treatment of other allergic disorders. While oral antihistamines (either OTC or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects. Available OTC.

TRIAMCINOLONE TOPICAL: Various

Class: Topical Corticosteroid

Dosage Forms. **Topical Cream:** 0.025%, 0.1%, 0.5%; **Topical Lotion:** 0.025%, 0.1%; **Topical Ointment:** 0.025%, 0.05%, 0.1%, 0.5%

Common FDA Label Indication, Dosing, and Titration.

1. Skin disorders: Apply thin layer topically to affected area daily or bid

Off-Label Uses. None

MOA. Triamcinolone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid.

Fougera generic 0.025% cream pictured

Drug Characteristics: Triamcinolone Topical

Dose Adjustment Hepatic	Not required	**Absorption**	Minimal absorption unless covering large surface area or covering areas lacking skin integrity
Dose Adjustment Renal	Not required	**Distribution**	Not absorbed
Dialyzable	Not dialyzable	**Metabolism**	Not absorbed
Pregnancy Category	C	**Elimination**	Not absorbed
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Triamcinolone Topical

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Ketalar	No

Drug Interactions: Triamcinolone Topical. None known

Adverse Reactions: Triamcinolone Topical

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
	Dry skin, burning sensation, stinging, pruritus/atrophy at site of administration	HPA suppression has been reported when used with occlusive dressings over larger surface areas

Efficacy Monitoring Parameters. Improvement in clinical signs of skin disorder.

Toxicity Monitoring Parameters. Seek medical attention if severe skin irritation or symptoms worsen after administration.

Key Patient Counseling Points. Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

Clinical Pearls. Large number of dosage formulations (foams, gels, shampoos, etc), both by prescription and OTC, are available. Oral and inhaled formulations, administered for systemic action, also available and used for similar indications as other oral corticosteroids. Application to large surface areas, prolonged use, and occlusive dressings increase risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption. TAC is an error-prone abbreviation; avoid.

TRIAMTERENE/HYDROCHLOROTHIAZIDE: Dyazide, Maxzide, Various

Class: Potassium Sparing/Thiazide Diuretic Combination

Dosage Forms. Oral Capsule: (Triamterene/Hydrochlorothiazide) 37.5 mg/25 mg, 50 mg/25 mg; **Oral Tablet:** (Triamterene/Hydrochlorothiazide) 37.5 mg/25 mg, 50 mg/25 mg, 75 mg/50 mg

Sandoz generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Edema: 37.5 mg/25 mg, 1-2 tablets or capsules po daily
2. Hypertension: 37.5 mg/25 mg, 1 tablet or capsule po daily, may titrate to 75 mg/50 mg po daily

Off-Label Uses. None

MOA. Triamterene acts directly from the distal tubular lumen on active sodium exchange for potassium and hydrogen, producing a mild diuresis that is independent of aldosterone concentration. Antihypertensive activity is inconsistent and less pronounced than with thiazides or spironolactone. Hydrochlorothiazide is a thiazide diuretic that increases sodium and chloride excretion by interfering with their reabsorption in the cortical diluting segment of the nephron; a mild diuresis of slightly concentrated urine results.

Drug Characteristics: Triamterene/Hydrochlorothiazide

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60-80% for hydrochlorothiazide, 30-70% for triamterene; food delays absorption
Dose Adjustment Renal	CrCl <25 mL/min, avoid use	**Distribution**	Hydrochlorothiazide is 40% protein bound, distribution limited to extracellular f uid space and kidneys; protein binding is 55-67% for triamterene
Dialyzable	Hydrochlorothiazide is not dialyzable; triamterene is removed by dialysis	**Metabolism**	Hydrochlorothiazide is not metabolized; extensive liver metabolism for triamterene
Pregnancy Category	C	**Elimination**	Hydrochlorothiazide is eliminated 50-70% unchanged in urine, with a half-life of 10-12 h; triamterene is eliminated in urine (5-10% unchanged), with a half-life of 4.3-6.5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to hydrochlorothiazide, sulfonamides or triamterene; concomitant use of potassium supplements, potassium-containing salt substitutes, or other potassium-sparing diuretics; or in patients with anuria, acute/ chronic renal insufficiency, or hyperkalemia	**Black Box Warnings**	Hyperkalemia

Medication Safety Issues: Triamterene/Hydrochlorothiazide

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
-25	No	No	No	Diazoxide, Dynacin	No

Drug Interactions: Triamterene/Hydrochlorothiazide

Typical Agents	Mechanism	Clinical Management
Aliskiren, ACE-Is, angiotensin-receptor blockers, potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
Eplerenone, potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium levels
Calcium supplements	Increased risk of hypercalcemia	Avoid concurrent use or monitor serum calcium levels
Antidiabetic medications	Decreased hypoglycemic effect	Monitor FBG
NSAIDs	Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr

Adverse Reactions: Triamterene/Hydrochlorothiazide

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Hypotension, dizziness, headache	Altered sense of taste, cramps, constipation, diarrhea, dry mouth, hyperglycemia, hyperuricemia, hypokalemia, hypomagnesemia, hyponatremia, impotence, loss of appetite, nausea, orthohypotension, photosensitivity, rash, tachycardia, urticaria, vomiting	Cardiac arrhythmias, hepatitis, hyperkalemia, gout, pancreatitis, Stevens-Johnson syndrome, decreased visual acuity

Efficacy Monitoring Parameters. Decreased BP, reductions in edema.

Toxicity Monitoring Parameters. Altered serum and urine electrolytes (calcium, magnesium, potassium, sodium), decreased renal function (increased SCr or decreased urine output), increased serum uric acid or blood glucose. Seek medical attention if skin rash, yellowing of eyes or skin, decreased urine output or symptoms of gout occur.

Key Patient Counseling Points. May cause dizziness. Avoid foods that are high in potassium, potassium supplements or potassium-containing salt substitutes. Avoid alcohol and NSAIDs. May cause photosensitivity; use sunscreen. Use with caution in patients with sulfonamide allergy.

Clinical Pearls. Safety and effectiveness not established in children.

TRIMETHOPRIM (TMP)/SULFAMETHOXAZOLE (SMZ): Bactrim, Septra, Various

Class: Sulfonamide Antibiotic

Dosage Forms. **Oral Tablet:** (SMZ/TMP) 400 mg/80 mg (single strength), 800 mg/160 mg (double strength); **Oral Suspension:** (SMZ/TMP) 200 mg/40 mg/5 mL

Amneal generic pictured

Common FDA Label Indication, Dosing, and Titration.

1. Acute infective exacerbation of COPD: 800 mg SMZ and 160 mg TMP po bid × 21 d
2. HIV infection, *Pneumocystis* pneumonia: 1600 mg SMZ and 320 mg TMP po bid × 21 d
3. HIV infection, *Pneumocystis* pneumonia, prophylaxis: Adults, 800 mg SMZ and 160 mg TMP po daily; Children ≥1 mo of age, 750 mg/m^2/d SMZ and 150 mg/m^2/d TMP in 2 divided doses po 3 times/wk on consecutive days
4. Traveler's diarrhea: 800 mg SMZ and 160 mg TMP po bid × 5 d
5. Urinary tract infection: Adult, 800 mg SMZ and 160 mg TMP po bid × 10-14 d; Children ≥2 mo of age, 8 mg/kg TMP component/d po bid × 10 d

Off-Label Uses.

1. Sinusitis: 800 mg SMZ and 160 mg TMP po bid × 10-14 d

MOA. SMZ competitively inhibits the synthesis of dihydropteric acid (an inactive folic acid precursor) in microorganisms. TMP inhibits the enzymatic reduction of dihydrofolic acid to tetrahydrofolic acid. The combination is active against many bacteria and *P. carinii*. TMP/SMZ has in vitro activity against methicillin-resistant *S. aureus* (MRSA), but clinical success has been variable and unpredictable.

Drug Characteristics: Trimethoprim/Sulfamethoxazole

Dose Adjustment Hepatic	Not required	**Absorption**	F = 90%, no effect of food on absorption
Dose Adjustment Renal	CrCl 15-30 mL/min, reduce dose by 50%; CrCl <15 mL/min, avoid, or reduce by 50% and increase interval to 24 h	**Distribution**	CSF
Dialyzable	Hemodialysis requires supplemental dose	**Metabolism**	Hepatic metabolism >90%, trimethoprim is CYP2C9 and CYP3A4/5 substrate. Trimethoprim is moderate inhibitor of CYP2C8 and CYP2C9
Pregnancy Category	D	**Elimination**	SMZ: renal elimination 10-30% with a half-life of 8-11 h; TMP: renal elimination 50-75% with a half-life of 6-17 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Individuals with G6PD deficiency are more likely to develop hemolytic anemia caused by SMZ/TMP
Contraindications	Hypersensitivity to sulfonamides, children <2 mo, pregnant patients at term, megaloblastic anemia due to folate deficiency	**Black Box Warnings**	None

Medication Safety Issues: Trimethoprim/Sulfamethoxazole

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
DS	No	No	No	Bacitracin, Bactine, Bactroban	No

Drug Interactions: Trimethoprim/Sulfamethoxazole

Typical Agents	Mechanism	Clinical Management
Antiarrhythmic agents, agents that prolong the QT interval	Increased risk of QT prolongation and other cardiac events	Avoid concurrent use or monitor carefully and consider dose reductions
CYP2C8 and CYP2C9 substrates	TMP is a CYP2C8 and CYP2C9 inhibitor, decreased metabolism of substrates, increases risk of substrate toxicity	Consider decreased dose of CYP2C8 and CYP2C9 substrates
CYP3A4/5 and CYP2C9 inducers	Increased TMP metabolism reduces TMP efficacy	Monitor and consider dose increases of TMP
CYP3A4/5 and CYP2C9 inhibitors	Decreased TMP metabolism increases risk of TMP toxicity	Monitor and consider dose decreases of TMP
Methotrexate	Increased toxicity of methotrexate through synergistic antifolate effects of TMP	Avoid concurrent use or consider methotrexate dose reduction or monitoring methotrexate levels

Adverse Reactions: Trimethoprim/Sulfamethoxazole

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea	Skin rash	Severe hypersensitivity, renal failure, hepatic failure, pancytopenia, arrhythmias, Stevens-Johnson syndrome, hyperkalemia, hypoglycemia, hemolytic anemia

Efficacy Monitoring Parameters. Resolution of signs of infection within 2-3 d. Decreased episodes of *Pneumocystis* pneumonia.

Toxicity Monitoring Parameters. Monitor potassium in those with concurrent ACI-Is. Monitor FPG with concurrent sulfonylureas. CBC monthly if using for PCP prophylaxis. Seek medical attention for severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

Key Patient Counseling Points. Complete full course of therapy. For the suspension, shake well and store at room temperature. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. May cause photosensitivity; use sunscreen. Maintain adequate hydration during therapy to prevent kidney complications.

Clinical Pearls. Avoid use in patients with G6PD deficiency (increased risk of hemolytic anemia). Preferred agent for *Pneumocystis* pneumonia prevention in HIV-infected patients when CD4 count is <200.

VALACYCLOVIR: Valtrex, Various

Class: Viral DNA Polymerase Inhibitor

Dosage Forms. Oral Tablet: 500 mg, 1000 mg

Ranbaxy generic 500 mg pictured

Common FDA Label Indication, Dosing, and Titration.

1. Genital herpes simplex: Initial episode, 1 g po bid × 10 d; recurrent, 500 mg bid × 3 d
2. Genital herpes simplex: Suppressive therapy, immunocompetent, 1 g po daily; HIV infected, 500 mg po bid
3. Herpes zoster, shingles: 1 g po tid × 7 d
4. Varicella: Children ≥2 y of age, 20 mg/kg po tid × 5 d
5. Herpes labialis (cold sores): 2 g po bid × 1 d

Off-Label Uses.

1. CMV prophylaxis in allogeneic stem cell transplant: 2 g po qid
2. Herpes simplex or varicella zoster in cancer patients: Prophylaxis, 500 mg po bid-tid; treatment, 1 g po tid

MOA. Valacyclovir is a prodrug of acyclovir. Acyclovir is an acyclic nucleoside analogue of deoxyguanosine that is selectively phosphorylated by the virus-encoded thymidine kinase to its monophosphate form. Cellular enzymes then convert the monophosphate to the active antiviral acyclovir triphosphate, which inhibits viral DNA synthesis by incorporation into viral DNA, resulting in chain termination. Acyclovir has potent activity against herpes simplex virus (HSV) I and II and varicella-zoster virus (VZV).

Drug Characteristics: Valacyclovir

Dose Adjustment Hepatic	Not required	**Absorption**	F = 10-20%, no effect of food on absorption
Dose Adjustment Renal	Moderate: increase interval to q8h; Severe: increase interval to q12h	**Distribution**	Placenta, CSF, kidney, brain, lung, heart
Dialyzable	Hemodialysis removes 60% of dose. Administer dose after dialysis	**Metabolism**	Hepatic; valacyclovir is rapidly and nearly completely converted to acyclovir and l -valine by first-pass effect; acyclovir is hepatically metabolized to a very small extent by aldehyde oxidase and by alcohol and aldehyde dehydrogenase
Pregnancy Category	B	**Elimination**	Renal elimination is 61-90% with a half-life of 2-3 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Valacyclovir

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	ValACYclovir	No	No	Acyclovir, valGANciclovir, vancomycin	No

Drug Interactions: Valacyclovir

Typical Agents	Mechanism	Clinical Management
Phenytoin, fosphenytoin, valproic acid	Decreased absorption and lower plasma concentration of phenytoin	Monitor phenytoin levels and adjust if necessary
Varicella virus vaccine	Decreased vaccine effectiveness via antagonism	Avoid concurrent use

Adverse Reactions: Valacyclovir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Malaise, headache, increased LFTs	Nausea, vomiting	Severe hypersensitivity, renal failure, TTP

Efficacy Monitoring Parameters. Resolution or prevention of clinical signs of infection (lesions).

Toxicity Monitoring Parameters. Seek medical attention if decreased urination, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Monitor CBC, LFTs, and SCr.

Key Patient Counseling Points. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If using for prophylaxis, this medication should reduce the number of breakouts.

Clinical Pearls. Not indicated for children <2 y of age. Use caution with concurrent nephrotoxins. Not for use in adults with chicken pox (varicella). Drug of choice for herpes zoster infection. Improved oral bioavailability over acyclovir, allowing bid dosing of valacyclovir (compared to 5 times/d dosing of acyclovir).

VALSARTAN: Diovan

Class: Angiotensin II Receptor Antagonist

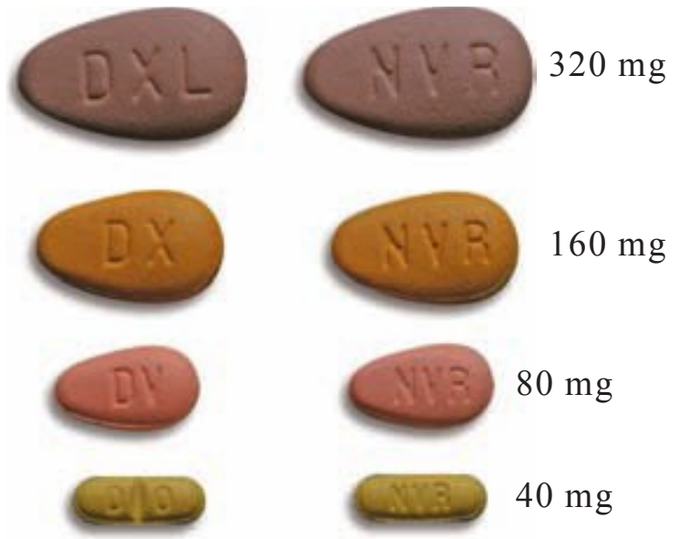
Dosage Forms. Oral Tablet: 40 mg, 80 mg, 160 mg, 320 mg

Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: 40 mg po bid, may titrate to 320 mg/d
2. Hypertension: 80-160 mg po daily, may titrate to 320 mg po daily
3. Myocardial infarction: 20 mg po bid, may titrate to 320 mg po daily

Off-Label Uses. None

MOA. Valsartan is a selective, reversible, competitive antagonist of the angiotension II receptor, which is responsible for the physiologic effects of angiotensin II, including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.



Novartis pictured

Drug Characteristics: Valsartan

Dose Adjustment Hepatic	Not required	**Absorption**	F = 25%, food does not affect absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 17 L; 95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal liver metabolism
Pregnancy Category	D	**Elimination**	Renal elimination is 7-13% and bile elimination is 89% with a half-life 6-9 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity, pregnancy	**Black Box Warnings**	Pregnancy

Medication Safety Issues: Valsartan

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Losartan, Valstar	No

Drug Interactions: Valsartan

Typical Agents	Mechanism	Clinical Management
Potassium-sparing diuretics	Increased risk of hypotension, hyperkalemia	Avoid concurrent use or monitor BP and serum potassium levels
ACE-Is	Increased risk of hypotension, hyperkalemia, nephrotoxicity	Avoid concurrent use or monitor BP, SCr, and potassium levels
Potassium supplements, salt substitutes	Increased risk of hyperkalemia and cardiac arrhythmias	Avoid concurrent use or monitor serum potassium level
NSAIDs	Decreased antihypertensive and natriuretic effect of valsartan, increased risk of nephrotoxicity	Avoid concurrent use or monitor BP and SCr
Diuretics	Increased risk of postural hypotension due to hypovolemia	Monitor BP; rise from seated position slowly

Adverse Reactions: Valsartan

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness	Back pain, cough, diarrhea, drowsiness, headache, hyperkalemia, hypotension, nausea, nephrotoxicity, rash, tachycardia	Angioedema, rhabdomyolysis

Efficacy Monitoring Parameters. Decreased BP, signs/symptoms of heart failure.

Toxicity Monitoring Parameters. Signs/symptoms of hypotension, tachycardia, angioedema (swelling of the face, eyes, lips, tongue, or throat), hyperkalemia (confusion, body weakness, uneven heartbeat, or numbness/tingling in hands or feet), reduction in urination, jaundice, or skin rash. Monitor vital signs, weight, LFTs.

Key Patient Counseling Points. Do not discontinue abruptly. Use potassium supplements or salt substitutes only under medical supervision. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Recommend avoiding alcohol and NSAIDs while taking this drug.

Clinical Pearls. ARBs can cause injury or death to the developing fetus when used during 2nd and 3rd trimesters. Therapy should be stopped as soon as possible when pregnancy is detected. In hypertensive patients with chronic kidney disease, either an ACE-I or ARB is recommended as first-line therapy to improve kidney outcomes. While ACE-Is are recommended as first-line therapy, in patients with heart failure or with ST-elevation myocardial infarctions, ARBs are recommended for patients unable to tolerate ACE-Is.

VARDENAFIL: Levitra, Staxyn

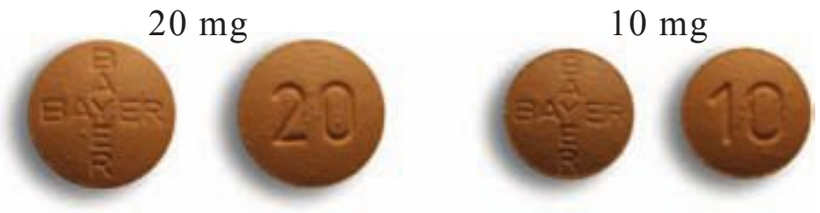
Class: Erectile Dysfunction Agent

Dosage Forms. Oral Tablet: 2.5 mg, 5 mg, 10 mg, 20 mg; **Oral Dispersible Tablet:** 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Erectile dysfunction: 10-20 mg po 60 min prior to anticipated sexual activity; *max* frequency is once daily

Off-Label Uses. None



Bayer pictured

MOA. Inhibition of phosphodiesterase type 5 (PDE5) by vardenafil enhances erectile function by increasing the amount of cyclic GMP. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increases blood flow into the corpus cavernosum.

Drug Characteristics: Vardenafil

Dose Adjustment Hepatic	Moderate hepatic impairment, decrease dose to 5-10 mg po prior to anticipated sexual activity; severe impairment, avoid use	**Absorption**	F = 15%, minimal food effect, water reduces the absorption of orally disintegrating tablet, take without liquid
Dose Adjustment Renal	Not required, but avoid use in dialysis patients	**Distribution**	Vd = 209 L; 95% protein bound
Dialyzable	Not dialyzable	**Metabolism**	90-95% hepatic, CYP3A4/5 substrate
Pregnancy Category	B	**Elimination**	<2-6% renal elimination with a half-life of 4-6 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to PDE inhibitors, concurrent nitrates	**Black Box Warnings**	None

Medication Safety Issues: Vardenafil

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Dispersible tablet	No	Sildenafil, tadalafil	No

Drug Interactions: Vardenafil

Typical Agents	Mechanism	Clinical Management
α-Adrenergic agents	Additive hypotension	Monitor for hypotension and consider dose reductions
CYP3A4/5 inducers	Increased vardenafil metabolism reduces vardenafil efficacy	Consider dose increases of vardenafil
CYP3A4/5 inhibitors	Decreased vardenafil metabolism increases risk of vardenafil toxicity	Reduce vardenafil dose to 2.5 mg q72h if concurrent strong inhibitors and 5 mg q24h if moderate inhibitors
Nitrates	Additive hypotension, potentially severe	Contraindicated

Adverse Reactions: Vardenafil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Flushing, headache	Nasopharyngitis, angina, chest pain, hypotension	Myocardial infarction, seizures, strokes, sudden hearing loss, priapism

Efficacy Monitoring Parameters. Improvement in sexual functioning.

Toxicity Monitoring Parameters. Seek medical attention if chest pain, erection lasting >4 h, tinnitus, dizziness, shortness of breath.

Key Patient Counseling Points. Take 60 min prior to anticipated sexual activity. Do not take more frequently than once q24h. The orally disintegrating tablet should be placed on tongue immediately upon removal from packaging; the tablet should be taken whole and not crushed or split, do not take with any liquids. Oral tablet can be taken without regard to food. If erection lasts >4 h, seek medical attention.

Clinical Pearls. The choice between tadalafil, sildenafil, or vardenafil is largely one of patient preference; tadalafil would be indicated in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of NO; the inhibition of PDE5 has no effect in the absence of sexual stimulation.

VARENICLINE: Chantix

Class: Smoking Cessation Agent

Dosage Forms. Oral Tablet: 0.5 mg, 1 mg

Common FDA Label Indication, Dosing, and Titration.

1. Smoking cessation: Initial dose, 0.5 mg po daily × 3 d, then 0.5 mg po bid × 4 d, then 1 mg po bid for the following 11 wk; may repeat additional 12 wk treatment if patient has not stopped smoking, and if patient has stopped, may increase likelihood of long-term abstinence

Off-Label Uses. None

MOA. Varenicline binds with high affinity and selectivity at α4β2 neuronal nicotinic acetylcholine receptors. Its efficacy in smoking cessation is believed to be the result of activity at α4β2 subtype of the nicotinic receptor where its binding produces agonist activity, while simultaneously preventing nicotine binding to these receptors.

Pfizer pictured

Drug Characteristics: Varenicline

Dose Adjustment Hepatic	Not required	**Absorption**	F = 99%, food has no effect on absorption
Dose Adjustment Renal	CrCl <30 mL/min, initial dose 0.5 mg po daily, and titrate up to 0.5 mg po bid; patients with end-stage renal disease, use with caution at *max* dose of 0.5 mg po daily	**Distribution**	20% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Minimal metabolism
Pregnancy Category	C	**Elimination**	Renal elimination is 92% unchanged with a half-life of 24 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	Neuropsychiatric effects, weigh risk/benefit

Medication Safety Issues: Varenicline

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Varenicline

Typical Agents	Mechanism	Clinical Management
Bupropion, H_2-antagonsits, quinolone antibiotics, trimethoprim	May increase varenicline serum concentration via unknown mechanisms	Monitor for adverse effects and consider dose decreases

Adverse Reactions: Varenicline

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dream disorder, nausea, headache, insomnia	Constipation, f atulence, vomiting	Abnormal behavior, suicidal thoughts, angioedema, hypersensitivity reactions, increased risk of accidents, increased risk of cardiovascular related events

Efficacy Monitoring Parameters. Abstinence from tobacco

Toxicity Monitoring Parameters. Seek medical attention if patient experiences severe abnormal behavior or suicidal thoughts.

Key Patient Counseling Points. Take drug after eating and with a full glass (8 oz) of water. If agitation, depressed mood, changes in behavior or thinking, or suicidal ideation, stop taking and contact health-care provider. May be used with other nicotine replacement products to help alleviate withdrawal from nicotine.

Clinical Pearls. Serious neuropsychiatric symptoms have been reported in patients being treated with varenicline. It may occur in patients without a history of psychiatric illness, although patients with bipolar disorder, depression, schizophrenia, or suicidal ideation appear to be at increased risk. Patients who continue to smoke are also at increased risk. FAA has banned its use in pilots and air traffic controllers. Patients and health-care providers should weigh the risks of taking varenicline against the benefits of smoking cessation. In a recent meta-analysis, there was an increased, but not statistically significant, incidence of major adverse cardiovascular events (a combined outcome of cardiovascular-related death, nonfatal myocardial infarction, and nonfatal stroke) in patients using varenicline when compared to placebo. Dispense with FDA-approved medication guide.

VARICELLA VACCINE, LIVE: Varivax

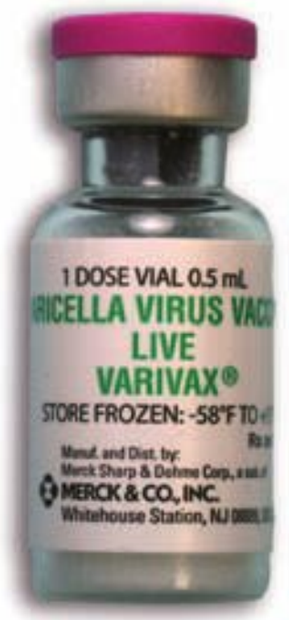
Class: Vaccine, Live, Viral

Dosage Forms. **Lyophilized Powder for Subcutaneous Injection:** 0.5 mL after reconstitution with diluent supplied; also available in combination with measles, mumps, and rubella vaccine

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of varicella infection: Adults, 2 doses separated by at least 4 wk; Children, 1 dose at 12 mo of age with a 2nd dose at 4-6 y of age, prior to entering school

Off-Label Uses. None



Merck pictured

Pregnancy Category	Contraindicated	**ADME**	None known
Lactation	Infant risk is likely minimal	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to varicella vaccine or a component of the vaccine; immunosuppression; pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Varicella Vaccine, Live

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	V-ZIG	No

Drug Interactions: Varicella Vaccine, Live

Typical Agents	Mechanism	Clinical Management
Aspirin, salicylates	Increased risk of Reye syndrome	Avoid giving salicylates to children for the 6 wk following varicella vaccine administration
Moderate- to high-dose corticosteroids	Immunosuppression and increased risk of infection by vaccine	Delay varicella vaccine administration until corticosteroid therapy has been discontinued
Immunosuppressing agents, including cyclosporine, cancer chemotherapy	Immunosuppression and increased risk of infection by vaccine	Delay varicella vaccine administration until immunosuppressive therapy has been discontinued
Immune globulin or blood products	Interference with immune response to live vaccines	Delay varicella vaccine administration for a period of time depending on type and dose of immune globulin or blood product

Adverse Reactions: Varicella Vaccine, Live

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence	Fever, rash, GI symptoms, lymphadenopathy	Thrombocytopenia, anaphylaxis, herpes zoster, febrile seizure

Efficacy Monitoring Parameters. Prevention of varicella infection, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

Toxicity Monitoring Parameters. Monitor for fever and rash.

Key Patient Counseling Points. Some children may experience mild fever and rash 7-10 d after vaccine administration.

Clinical Pearls. Varicella vaccine contains the same vaccine virus as zoster vaccine, but the doses are dramatically different and are not interchangeable. Indicators of varicella immunity include birth in the United States before 1980, physician-documented history of disease, laboratory evidence of immunity, or 2 doses of varicella vaccine after 12 mo of age. Individuals born in the United States before 1980 can be considered immune to varicella unless health-care personnel, immunocompromised, or pregnant woman. Transmission of the vaccine virus to susceptible individuals without serious lasting consequences has been documented. If not administered simultaneously, varicella vaccine must be separated by at least 4 wk from other live vaccines. Febrile seizure is more common with the combination measles-mumps-rubella-varicella vaccine compared to MMR and varicella vaccines given as separate injections. Pregnant women exposed to varicella should not receive vaccine; instead, should receive varicella zoster immune globulin.

VENLAFAXINE: Effexor, Effexor XR, Various

Class: Antidepressant, Serotonin/Norepinephrine Reuptake Inhibitor

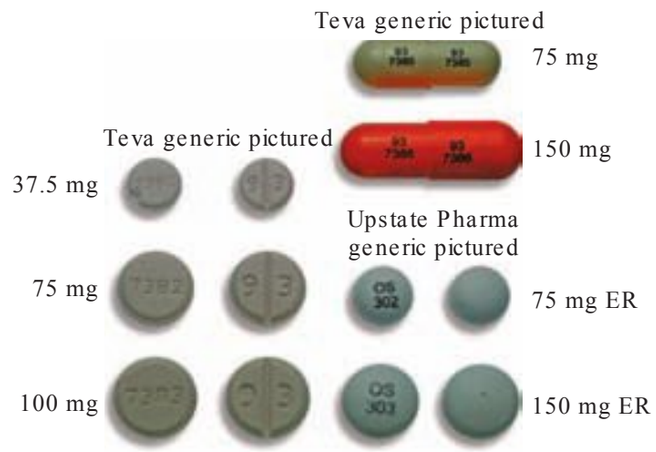
Dosage Forms. **Oral Capsule, Extended Release:** 37.5 mg, 75 mg, 150 mg; **Oral Tablet:** 25 mg, 37.5 mg, 50 mg, 75 mg, 100 mg; **Oral Tablet, Extended Release:** 37.5 mg, 75 mg 150 mg, 225 mg

Common FDA Label Indication, Dosing, and Titration.

1. Generalized anxiety disorder: Extended release, 37.5-75 mg po daily, may titrate to 225 mg/d
2. Depression: Immediate release, 75 mg po daily in 2-3 divided doses, may titrate to 225 mg/d; extended release, 37.5-75 mg po daily, may titrate to 225 mg/d
3. Panic disorder: Extended release, 37.5 mg po daily × 7 d, then 75 mg po daily, then may titrate to 225 mg/d
4. Social anxiety disorder: Extended release, 75 mg po daily

Off-Label Uses.

1. OCD: Immediate release, 25 mg po tid, may titrate to 300 mg/d
2. Hot flashes: 37.5-75 mg po daily



MOA. Potent reuptake inhibitor of serotonin and norepinephrine but lacks effects on muscarinic, α-adrenergic, or histamine receptors.

Drug Characteristics: Venlafaxine

Dose Adjustment Hepatic	Mild-moderate liver impairment, decrease dose by 25-50%; severe impairment, avoid	**Absorption**	F = 12.6% (immediate release), 45% (extended release); no effect of food on absorption
Dose Adjustment Renal	Mild-moderate renal impairment, decrease dose by 25-50%; dialysis, decrease dose by 50%	**Distribution**	Vd = 7.5 L; 27-30% protein bound
Dialyzable	Not dialyzable	**Metabolism**	87% hepatic, CYP2D6 and CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination is 87% (82% as metabolites, 5% unchanged) with a half-life of 5 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	Venlafaxine metabolized to an active metabolite by CYP2D6. Poor CYP2D6 metabolizers have higher concentrations of venlafaxine, but similar clinical effects.
Contraindications	Hypersensitivity; MAOIs	**Black Box Warnings**	Suicidal ideation

Medication Safety Issues: Venlafaxine

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
XR	No	Do not crush, chew ER formulations. Capsule may be sprinkled on food	No	No	No

Drug Interactions: Venlafaxine

Typical Agents	Mechanism	Clinical Management
Agents that prolong the QT interval	Increased risk of cardiotoxicity	Avoid concurrent use
Anticoagulants, antiplatelet drugs, NSAIDs	Increased risk of bleeding	Monitor for bleeding, avoid concurrent use if possible
CYP3A4/5, CYP2D6 inhibitors	Decreased venlafaxine metabolism increases risk of venlafaxine toxicity	Avoid concurrent use or monitor for adverse effects; consider dose decrease
CYP3A4/5 inducers	Increased venlafaxine metabolism reduces venlafaxine efficacy	Monitor for efficacy and consider dose increase
Dextroamphetamine, SSRIs, sumatriptan, tramadol, trazodone, zolmitriptan, linezolid	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome, linezolid contraindicated

Adverse Reactions: Venlafaxine

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, headache, insomnia, nausea, somnolence, xerostomia	Anxiety, asthenia, bleeding, blurred vision, diaphoresis, hypertension, hyponatremia, hypercholesterolemia, sexual dysfunction, tremor, vomiting, weight loss, sexual dysfunction	GI hemorrhage, hepatotoxicity, serotonin syndrome, suicidal thoughts

Efficacy Monitoring Parameters. Improvement in depression, anxiety, and panic symptoms.

Toxicity Monitoring Parameters. Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding; signs/symptoms of serotonin syndrome; monitor BP, LFT, serum cholesterol levels, in case of severe impairment at baseline and periodically during therapy; signs/symptoms of hyponatremia, especially in patients on concomitant diuretics, volume-depleted patients, and elderly.

Key Patient Counseling Points. Take venlafaxine with food, but avoid alcohol. Extended-release capsules and tablets should be swallowed whole. Contents of extended-release capsules may be sprinkled on food and swallowed without chewing, followed by water. Symptomatic improvement may not be evident for a few weeks. Do not discontinue drug abruptly, as this may precipitate withdrawal symptoms such as dysphoric mood, irritability, and agitation. Avoid activities requiring mental alertness; may cause dizziness or somnolence.

Clinical Pearls. May convert to extended-release capsules or tablets based on nearest equivalent dose (mg/d) of stable immediate-release dose.

VERAPAMIL: Calan, Calan SR, Isoptin SR, Various

Class: Calcium Channel Blocker

Dosage Forms. **Oral Tablet:** 40 mg, 80 mg, 120 mg; **Oral Tablet, Extended Release:** 120 mg, 180 mg, 240 mg; **Oral Capsule, Extended Release:** 100 mg, 120 mg, 180 mg, 200 mg, 240 mg, 300 mg, 360 mg

Common FDA Label Indication, Dosing, and Titration.

1. Angina: Immediate release, 80-120 mg po tid; extended release, 180 mg po daily hs, may titrate to 480 mg po daily
2. Atrial arrhythmia or paroxysmal supraventricular tachycardia prophylaxis: Immediate release, 240-320 mg/d in 3-4 divided doses, may titrate to 480 mg/d in nondigitalized patients
3. Hypertension: Immediate release, 80 mg po tid, may titrate to 360-480 mg/d; extended release, 180-200 mg po daily hs, may titrate to 400-480 mg po daily; sustained release 180 mg po daily in am, may titrate to 240-480 mg/d

Off-Label Uses. None

MOA. Inhibits calcium "slow channels" on vascular smooth muscle and myocardium producing relaxation of muscle and vasodilation. Increases myocardial oxygen delivery and slow conduction through the AV node.

Mylan generic pictured


Mylan generic 120 mg pictured


Teva generic 240 mg pictured

Drug Characteristics: Verapamil

Dose Adjustment Hepatic	Reduce dose by 20-50%	**Absorption**	F = 13-65%; no affect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 3.89 L/kg; 86-94% protein bound
Dialyzable	Not dialyzable	**Metabolism**	70% and occurs by CYP3A4/5, moderate inhibitor of CYP3A4/5
Pregnancy Category	C	**Elimination**	Renal elimination is 70% (3-4% unchanged) and 9-16% in feces, with a half-life of 4-12 h
Lactation	Compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to verapamil; symptomatic hypotension (systolic BP <90 mm Hg); 2nd- or 3rd-degree AV heart block, sick sinus syndrome; severe left ventricular dysfunction (ejection fraction <30%)	**Black Box Warnings**	None

Medication Safety Issues: Verapamil

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
SR, PM	No	Do not crush or chew sustained or extended-release products	Yes (IV only)	Colace	No

Drug Interactions: Verapamil

Typical Agents	Mechanism	Clinical Management
Amiodarone, beta-blockers	Increased risk of bradycardia, heart block (amiodarone), sinus arrest, AV conduction disturbances (beta-blockers)	Avoid concurrent use in patients with sick sinus syndrome or AV block or monitor BP and HR
CYP3A4/5 inhibitors	Decreased verapamil metabolism increases the risk of verapamil toxicity	Avoid concurrent use or monitor for adverse effects
CYP3A4/5 inducers	Increased verapamil metabolism decreases verapamil efficacy	Monitor for efficacy; consider dose increase
CYP3A4/5 substrates	Increased substrate concentration and increased substrate toxicity via inhibition of CYP3A4/5 by verapamil	Avoid narrow therapeutic index concurrent medications; otherwise monitor and consider dose reductions
Disopyramide	May aggravate or precipitate heart failure	Avoid giving disopyramide 48 h before or for 24 h after verapamil

Adverse Reactions: Verapamil

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Gingival hyperplasia	Bradyarrhythmia, constipation, dizziness, fatigue, headache, hypotension, indigestion, nausea, palpitations, peripheral edema, rash, syncope, elevated liver enzymes	Congestive heart failure, heart block, hepatotoxicity, pulmonary edema

Efficacy Monitoring Parameters. Decreased BP, improvement in HR and rhythm, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of nitroglycerin for chest pain.

Toxicity Monitoring Parameters. Signs/symptoms of heart failure, decreased HR, signs/symptoms of liver toxicity. Exacerbations of angina pectoris or acute coronary insufficiency; while tapering chronic therapy, especially in patients with ischemic heart disease. Monitor LFTs, ECG, and vital signs.

Key Patient Counseling Points. Do not crush or chew extended-release products. Contents of extended-release capsules may be sprinkled on food and swallowed without chewing, followed by water. Instruct patient to report symptomatic hypotension, bradyarrhythmia, peripheral edema, or syncope. Advise patients against sudden discontinuation of drug, as this may precipitate hypertensive rebound/crisis. Rise slowly from a sitting or lying position to avoid dizziness.

Clinical Pearls. Not approved in children <18 y of age.

VILAZODONE: Viibryd

Class: Antidepressant, SSRI/5-HT_{1A} Receptor Partial Agonist

Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg

Common FDA Label Indication, Dosing, and Titration.

1. Depression: Adults, 10 mg po once daily × 7 d, then 20 mg po once daily × 7 d, then 40 mg po daily

Off-Label Uses. None

MOA. Vilazodone inhibits CNS neuron serotonin uptake, with minimal or no effect on reuptake of norepinephrine or dopamine. It binds selectively with high affinity to 5-HT_{1A} receptors (altered in depression and anxiety patients) and is a 5-HT_{1A} receptor partial agonist.

Drug Characteristics: Vilazodone

Dose Adjustment Hepatic	Not required	**Absorption**	F = 72% with food; food increases AUC 50%
Dose Adjustment Renal	Not required	**Distribution**	Widely distributed; 96-99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	Hepatic, CYP3A4/5 substrate
Pregnancy Category	C	**Elimination**	Renal elimination (primarily as metabolites), with a half-life of 25 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity; concurrent use of MAOI	**Black Box Warnings**	Suicidal thinking and suicidal behavior

Medication Safety Issues: Vilazodone

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Lurasidone, paliperidone, risperidone, ziprasidone	No

Drug Interactions: Vilazodone

Typical Agents	Mechanism	Clinical Management
CYP3A4/5 inducers	Increased vilazodone metabolism reduces vilazodone effectiveness	Monitor and consider dose increases of vilazodone
CYP3A4/5 inhibitors	Decreased vilazodone metabolism increases risk of vilazodone toxicity	Monitor and consider dose decreases of vilazodone
Triptans, SSRIs, dextroamphetamine, tramadol, MAOIs	Increased risk of serotonin syndrome	Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination)

Adverse Reactions: Vilazodone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Diarrhea, nausea	Palpitations, dizziness, insomnia, fatigue, drowsiness, restlessness, migraine, sedation, xerostomia, arthralgia, sexual dysfunction	Hyponatremia, serotonin syndrome

Efficacy Monitoring Parameters. Reduction in symptoms of depression.

Toxicity Monitoring Parameters. Signs and symptoms of withdrawal upon abrupt dose reduction or discontinuation. Signs and symptoms of serotonin syndrome or akatheisia. Monitor for suicidal ideation.

Key Patient Counseling Points. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient that symptomatic improvement may not be seen for a few weeks. Advise patient against sudden discontinuation of drug. Patient may take with or without food, but should always take drug consistently. Patient should not drink alcohol or large amounts of grapefruit juice while taking this drug. Avoid concomitant use with MAO inhibitors.

Clinical Pearls. Safety and efficacy not established in pediatric patients <18 y of age.

WARFARIN: Coumadin, Various

Class: Anticoagulant, Vitamin K Antagonist

Dosage Forms. Oral Tablet: 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, 10 mg

Common FDA Label Indication, Dosing, and Titration.

1. Multiple FDA-labeled indications, all dosed similarly, including atrial fibrillation; myocardial infarction; prosthetic cardiac valve component embolism; pulmonary embolism; thrombosis, postmyocardial infarction; venous thromboembolism: Initial, 2-5 mg po daily, adjust dose based on INR; usual maintenance 2-10 mg po daily

Off-Label Uses.

1. Prevention of transient ischemic attacks: Initial, 2-5 mg po daily, adjust dose based on INR; usual maintenance 2-10 mg po daily

MOA. Warfarin prevents the conversion of vitamin K back to its active form from vitamin K epoxide. This impairs formation of the vitamin K–dependent clotting factors II, VII, IX, and X (prothrombin) and proteins C and S (physiologic anticoagulants).

Taro generic pictured

Drug Characteristics: Warfarin

Dose Adjustment Hepatic	Initial dose should be <5 mg po daily, adjust dose based on INR	**Absorption**	F = 100%; no effect of food on absorption
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.14 L/kg; protein binding 99%
Dialyzable	Not dialyzable	**Metabolism**	>90% hepatic, CYP2C9 substrate
Pregnancy Category	X	**Elimination**	Renal elimination of metabolites is 92% with a half-life of 20-60 h
Lactation	Compatible	**Pharmacogenetics**	CYP2C9 and VKORC1 genetic variation may be useful in initial dosing of warfarin
Contraindications	Hypersensitivity, bleeding tendencies recent or potential surgery, uncontrolled hypertension; pericarditis or pericardial effusion; bacterial endocarditis; noncompliant patients, eclampsia/preeclampsia, threatened abortion, pregnancy	**Black Box Warnings**	Bleeding

Medication Safety Issues: Warfarin

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	Yes	Avandia	No

Drug Interactions: Warfarin

Typical Agents	Mechanism	Clinical Management
Agents with a risk of bleeding, antiplatelet agents, direct thrombin inhibitors, NSAIDs, acetaminophen, others	Additive effects and increased risk of bleeding	Monitor for signs/symptoms of bleeding; measure INR and avoid concurrent use if possible
CYP2C9 inhibitors	Decreased warfarin metabolism increases risk of warfarin toxicity	Use caution with concomitant therapy; monitor INR and adjust warfarin dose
CYP2C9 inducers	Increased warfarin metabolism decreases warfarin efficacy	Use caution with concomitant therapy; monitor INR and adjust warfarin dose
Sucralfate	Inhibits warfarin absorption	Separate administration by 1-2 h

Adverse Reactions: Warfarin

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Bleeding	Anemia, epistaxis, rash	Hemorrhage (particularly GI tract), purple toe syndrome, tissue necrosis

Efficacy Monitoring Parameters. Measure initial INR after the first 2-3 doses and subsequently at intervals no longer than every 4 wk, once stable dose has been achieved; may monitor every 12 wk in stable patients, use clinical judgment; patients at high risk of bleeding require more frequent monitoring. INR target and therapeutic range depend on indication. Atrial fibrillation/atrial flutter: target 2.5 (range 2-3); prosthetic heart valves: target 2.5 (range 2-3); mechanical mitral or aortic valve: target 3 (range 2.5-3.5); myocardial infarction, ST segment elevation: target 3 (2.5-3.5, with aspirin); venous thromboembolism, prophylaxis and treatment (including pulmonary embolism, DVT, hip/knee arthroplasty): target 2.5 (range 2-3).

Toxicity Monitoring Parameters. Signs/symptoms of bleeding, CBC, LFT, stool guaiac test.

Key Patient Counseling Points. Report signs/symptoms of hemorrhage, skin and tissue necrosis. Avoid situations/activities in which cuts, bruising, or injury is likely to occur. Many significant drug-drug interactions, consult health-care professional prior to new prescription or OTC use. Avoid alcohol, cranberry products, and drastic changes in vitamin K consumption from diet (cruciferous vegetables).

Clinical Pearls. Patients often managed in pharmacist-run anticoagulation clinics. Consult local protocols. Excessive anticoagulation with warfarin can be corrected with vitamin K. Pharmacogenetic testing for initial dosing of warfarin decreases the time required to achieve a therapeutic INR, but improved clinical efficacy and decreased adverse effects have not been achieved; therefore pharmacogenetic testing is not routine.

ZIPRASIDONE: Geodon

Class: Second-Generation Antipsychotic

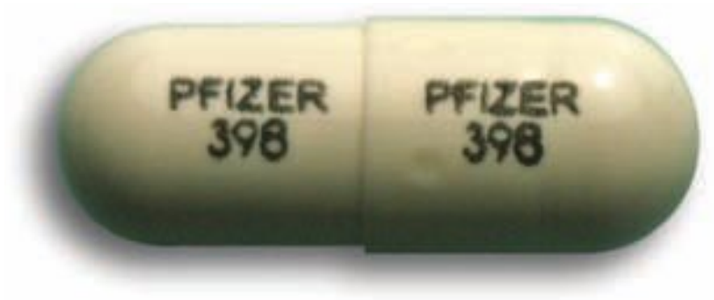
Dosage Forms. Oral Capsule: 20 mg, 40 mg, 60 mg, 80 mg

Common FDA Label Indication, Dosing, and Titration.

1. Bipolar disorder, acute manic or mixed episodes, monotherapy, or adjunct to lithium or valproate: 40-80 mg po bid
2. Schizophrenia: 20 mg po bid, may titrate to 40-100 mg bid

Off-Label Uses.

1. Psychosis and agitation related to Alzheimer dementia: 20-80 mg po bid



Pfizer 60 mg pictured

MOA. Ziprasidone is an atypical antipsychotic drug with a very high ratio of 5-HT_{2A} to dopamine-2 blockade, suggesting a very low risk of extrapyramidal effects. In addition, it is a 5-HT_{1A} agonist and inhibits reuptake of both serotonin and norepinephrine like antidepressants. The clinical value of the latter 2 effects is not established.

Drug Characteristics: Ziprasidone

Dose Adjustment Hepatic	Not required	**Absorption**	F = 60%; food increases absorption twofold
Dose Adjustment Renal	Not required	**Distribution**	Vd = 1.5 L/kg; >99% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>95% and occurs by aldehyde oxidase
Pregnancy Category	C	**Elimination**	Renal elimination is 20% (<1% unchanged) and 66% in feces (<4% unchanged), with a half-life of 7 h
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to ziprasidone; acute or recent myocardial infarction; uncompensated heart failure; QT prolongation, including congenital long QT syndrome; concomitant administration of other drugs that cause QT prolongation	**Black Box Warnings**	Elderly patients with dementia are at increased risk of death

Medication Safety Issues: Ziprasidone

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	TraZODone	Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others

Drug Interactions: Ziprasidone

Typical Agents	Mechanism	Clinical Management
Agents that increase QT interval	Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest)	Concomitant use contraindicated
Carbamazepine	Decreased ziprasidone concentrations	Use with caution; monitor ziprasidone efficacy

Adverse Reactions: Ziprasidone

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, extrapyramidal disease, headache, nausea, somnolence	Abnormal vision, akathisia, anxiety, asthenia, constipation, diarrhea, indigestion, rash, spasmodic movement, tremor, weight gain, vomiting, xerostomia	Bone marrow depression, diabetes, neuroleptic malignant syndrome, prolonged QT interval, syncope, tardive dyskinesia, torsades de pointes

Efficacy Monitoring Parameters. Improvement in signs and symptoms of schizophrenia or manic or mixed episodes associated with bipolar disorder.

Toxicity Monitoring Parameters. FPG and CBC at baseline and periodically during therapy; patients at high risk for suicide should be closely supervised during therapy. Monitor vital signs, including temperature.

Key Patient Counseling Points. Take with food but avoid alcohol. Avoid activities requiring mental alertness or coordination, as this medicine may cause dizziness and somnolence. Use caution with activities leading to an increased core temperature, such as strenuous exercise, exposure to extreme heat, or dehydration. Rise slowly from a sitting/supine position, as drug may cause orthostatic hypotension. Report signs/symptoms of bradycardia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome.

Clinical Pearls. Safety and effectiveness in pediatric patients have not been established. Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Not approved for dementia-related psychosis.

ZOLPIDEM: Ambien, Various

Class: Nonbarbiturate Hypnotic

C-IV

Dosage Forms. **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet, Extended Release:** 6.25 mg, 12.5 mg; **Sublingual Tablet:** 1.75 mg, 3.5 mg, 5 mg, 10 mg; **Oromucosal Spray:** 5 mg/actuation

Common FDA Label Indication, Dosing, and Titration.

1. Insomnia, short-term treatment: Immediate release, spray or sublingual, 1.75-5 mg (females), 3.5-10 mg (males) po daily hs; extended release, 6.25 mg (females), 6.25-12.5 mg (males) po daily hs

Off-Label Uses. None

MOA. Zolpidem binds the benzodiazepine receptor but is structurally different from a benzodiazepine. Sedative and hypnotic effects due to increased chloride conductance, neuronal hyperpolarization, inhibition of action potential, and decrease in neuronal excitability.

Wockhardt generic 5 mg pictured

Drug Characteristics: Zolpidem

Dose Adjustment Hepatic	Moderate or severe hepatic failure: reduce dose by 50%	**Absorption**	F = 70%, food decreases absorption; Cmax and AUC increased ~45% in females
Dose Adjustment Renal	Not required	**Distribution**	Vd = 0.54 L/kg; 93% protein bound
Dialyzable	Not dialyzable	**Metabolism**	>99% hepatic, CYP3A4/5 (60%) and CYP2C9 (20%) substrate, other CYPs with small contributions
Pregnancy Category	C	**Elimination**	Renal elimination is <1% with a half-life of 3 h
Lactation	Usually compatible	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity	**Black Box Warnings**	None

Medication Safety Issues: Zolpidem

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
CR	No	Do not crush or chew ER tablets or SL tablet	No	Abilify, Ativan	Avoid chronic use (>90 d)

Drug Interactions: Zolpidem

Typical Agents	Mechanism	Clinical Management
Benzodiazepines, CNS depressants, TCAs	Additive CNS depression	Avoid if possible and consider dose reductions of both agents
Bupropion, desipramine, sertraline, venlafaxine	Increased risk of hallucinations	Avoid if possible and consider dose reductions of both agents
CYP3A4/5 inhibitors	Decreased zolpidem metabolism increases risk of zolpidem toxicity	Avoid concurrent use or consider dose reductions
CYP3A4/5 inducers	Increased zolpidem metabolism decreases efficacy	Avoid concurrent use or consider dose increases

Adverse Reactions: Zolpidem

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Dizziness, drowsiness, headache	Chest pain, blurred vision, nausea, diarrhea, confusion, impaired motor coordination, somnolence	Tachycardia, complex behavior, abnormal thinking, behavior changes, anaphylaxis, worsening of depression, angioedema, drug dependence

Efficacy Monitoring Parameters. Improved ability to fall asleep and sleep through the night. Increased daytime alertness.

Toxicity Monitoring Parameters. Seek medical attention if severe drowsiness, thoughts of suicide, allergic reaction, irregular respiratory rate, fast or irregular heartbeat.

Key Patient Counseling Points. Take on an empty stomach. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol. Take immediately prior to bedtime. May interfere with complex behaviors (driving, talking on phone, etc, while not fully awake); bed partner should monitor irregular respiratory rate for abnormalities.

Clinical Pearls. Not for long-term use (usually 7-10 d only). Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use of CNS depressants with caution, may have additive effects. Recommended dose for immediate-release products was recently lowered from 10 to 5 mg and from 12.5 to 6.25 mg for extended-release products in women to reduce risk of morning somnolence. Dispense with medication safety guide.

ZOSTER VACCINE, LIVE: Zostavax

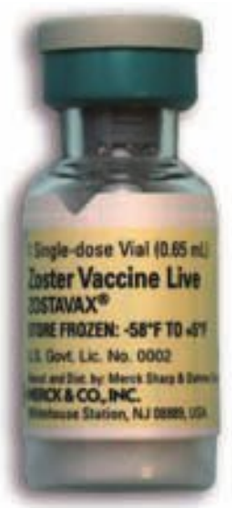
Class: Vaccine, Live, Viral

Dosage Forms. Suspension for Subcutaneous Injection: 0.65 mL after reconstitution

Common FDA Label Indication, Dosing, and Titration.

1. Prevention of herpes zoster (zoster, shingles): Adults, single dose for adults ≥50 y of age

Off-Label Uses. None



Merck pictured

Drug Characteristics: Zoster Vaccine, Live

Pregnancy Category	Contraindicated	**ADME**	None known
Lactation	Weigh risks and benefits	**Pharmacogenetics**	None known
Contraindications	Hypersensitivity to zoster vaccine or a component of the vaccine; immunosuppression; pregnancy	**Black Box Warnings**	None

Medication Safety Issues: Zoster Vaccine, Live

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	Zovirax	No

Drug Interactions: Zoster Vaccine, Live

Typical Agents	Mechanism	Clinical Management
Moderate- to high-dose corticosteroids	Immunosuppression and increased risk of infection by vaccine virus	Delay zoster vaccine administration until corticosteroid therapy has been discontinued
Immunosuppressing agents; azathioprine, chemotherapy, cyclosporine	Immunosuppression and increased risk of infection by vaccine virus	Delay zoster vaccine administration until immunosuppressive therapy has been discontinued
Pneumococcal polysaccharide vaccine (PPSV23)	Immunological interference	Concomitant administration with PPSV23 lowers antibody concentrations to zoster vaccine; clinical consequences are unknown and no change in efficacy observed if administered simultaneously; separate vaccines by 4 wk if follow-up assured
Antiviral agents	Neutralization of the vaccine virus; theoretical	Hold antiviral therapy for 1 d prior to and 14 d following zoster vaccine administration

Adverse Reactions: Zoster Vaccine, Live

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Injection site reactions, including erythema and soreness	Headache, f u-like symptoms	Anaphylaxis, Guillain-Barré syndrome

Efficacy Monitoring Parameters. Prevention of herpes zoster (shingles).

Toxicity Monitoring Parameters. None.

Key Patient Counseling Points. About 1 in 3 individuals develops a rash at the injection site, which resolves after a few days with no treatment. The zoster vaccine is not 100% effective in preventing zoster. However, the disease and its consequences are less severe in immunized individuals who develop zoster.

Clinical Pearls. A history of chicken pox need not be obtained prior to zoster vaccine administration as birth before 1980 is considered evidence of varicella immunity. Consider administering the vaccine to 50-59-year-olds who are anticipating immunosuppressive therapy and those with HIV. Single dose recommended for all adults aged ≥60 y without regard to history of shingles; zoster vaccine may be administered to individuals on inhaled, topical, or intra-articular steroids or low-dose oral steroids; treated with low-dose methotrexate (<0.4 mg/kg/wk) or 6-mercaptopurine (<1.5 mg/kg/d), anticipating immunosuppressive therapy if vaccine can be administered at least 14 d prior or on antiviral therapy if it is stopped 1 d prior to vaccine administration and held for 14 d. Zoster vaccine can be administered to individuals with HIV if no manifestations of AIDS and CD4 count >200/mm^3.

SOFOSBUVIR: Sovaldi

Class: Polymerase Inhibitor (Anti-HCV)

Dosage Forms. Oral Tablet: 400 mg

Common FDA Label Indication, Dosing, and Titration.

1. Chronic hepatitis C (CHC) infection in monoinfected (HCV) or coinfected (HCV/HIV-1) patients: 400 mg po daily with concomitant ribavirin and/or peginterferon alfa (treatment regimen and duration based on HCV genotype and/or clinical scenario); HCV genotype 1 or 4, treat for 12 wk with ribavirin and peginterferon alfa; HCV genotype 2, treat for 12 wk with concomitant ribavirin; HCV genotype 3, treat for 24 wk with concomitant ribavirin
2. Patients with hepatocellular carcinoma awaiting liver transplantation: 400 mg po daily with concomitant ribavirin for 48 wk or until the time of liver transplantation, whichever occurs first

Off-Label Uses. None

MOA. A direct-acting antiviral agent against the hepatitis C virus. It inhibits HCV NS5B RNA-dependent RNA polymerase, essential for viral replication, and acts as a chain terminator.

Drug Characteristics: Sofosbuvir

Dose Adjustment Hepatic	Not required	**Absorption**	F is unknown; food has no effect on Cmax or AUC
Dose Adjustment Renal	Primary metabolite accumulates in renal dysfunction, but no dose adjustments are required	**Distribution**	Protein binding 61-65%
Dialyzable	Yes, hemodialysis	**Metabolism**	Hepatic, P-glycoprotein substrate
Pregnancy Category	B (X in combination with ribavirin)	**Elimination**	Renal, 78% as active metabolite; half-life of parent compound, 0.4 h; half-life of active metabolite, 27 h
Lactation	Not recommended	**Pharmacogenetics**	HCV genotype determines treatment regimen
Contraindications	Because of ribavirin risk, do not use in pregnant women, or men whose female partners are pregnant	**Black Box Warnings**	None

Medication Safety Issues: Sofosbuvir

Suffixes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	No	No	No	No

Drug Interactions: Sofosbuvir

Typical Agents	Mechanism	Clinical Management
P-glycoprotein inhibitors	Decreased sofosbuvir transport increases risk of sofosbuvir toxicity	Monitor carefully and consider sofosbuvir dose reduction
P-glycoprotein inducers	Increased sofosbuvir transport decreases sofosbuvir efficacy	Avoid concurrent use, or monitor carefully and consider sofosbuvir dose increases

Adverse Reactions: Sofosbuvir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Fatigue, headache, insomnia, chills, pruritus, rash, nausea, anemia	Diarrhea, thrombocytopenia increased LFTs	Pancytopenia, depression, suicidality

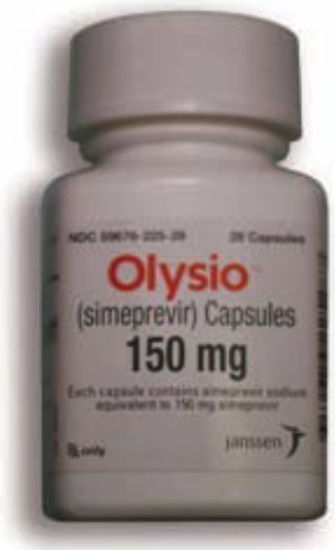
Efficacy Monitoring Parameters. Improvement in signs and symptoms of hepatitis C infection. Monitor SCr and LFTs. Serum hepatitis C viral RNA levels prior and during treatment.

Toxicity Monitoring Parameters. In female patients and female partners of male patients, pregnancy tests should be done prior to and during treatment.

Key Patient Counseling Points. Must be taken with ribavirin, and depending on viral genotype, peginterferon alfa. Pregnancy warnings (due to ribavirin risk) for female patients and female partners of male patients.

Clinical Pearls. Astronomically expensive (approximately $80,000 per 12-wk course of therapy). Must be used in combination with other treatments based on the viral genetic category (not the patient's genetic make-up). In patients who cannot tolerate interferon, off-label regimens have been recommended that include sofosbuvir and ribavirin alone. Off-label regimens are also recommended in patients with HCV genotype 5 and 6, and those patients who fail on treatments with sofosbuvir and/or ribavirin and peginterferon alfa.

SIMEPREVIR: Olysio



Class: Polymerase Inhibitor (Anti-HCV)

Dosage Forms. Oral Capsule: 150 mg

Common FDA Label Indication, Dosing, and Titration.

1. CHC infection in patients with HCV genotype 1a: 150 mg po daily with food as part of combination regimen with concomitant ribavirin and peginterferon alfa (duration 12 wk, followed by 12 or 36 additional weeks of peginterferon alfa and ribavirin alone depending on prior response status), or with sofosbuvir (duration 12 wk in patients without cirrhosis, or 24 wk in patients with cirrhosis; screening patients with HCV genotype 1a infection for the presence of virus with the NS3 Q80K polymorphism at baseline is strongly recommended, and alternative therapy should be considered for patients infected with HCV genotype 1a containing the Q80K polymorphism

Off-Label Uses. None

MOA. A direct-acting antiviral agent against the hepatitis C virus. It inhibits HCV NS3/4A protease, essential for viral replication, and acts as a chain terminator.

Drug Characteristics: Simeprevir

Dose Adjustment Hepatic	Not required	**Absorption**	F is unknown; food enhances AUC
Dose Adjustment Renal	Not required	**Distribution**	Protein binding >99%
Dialyzable	Unknown	**Metabolism**	Hepatic, CYP3A4/5 and P-glycoprotein substrate
Pregnancy Category	C (X in combination with ribavirin)	**Elimination**	Feces, 91%; <1% eliminated renally; half-life is 10-13 h
Lactation	Not recommended	**Pharmacogenetics**	HCV genotype determines treatment regimen
Contraindications	Because of ribavirin risk, do not use in pregnant women, or men whose female partners are pregnant	**Black Box Warnings**	None

Medication Safety Issues: Simeprevir

Suf xes	Tall Man Letters	Do Not Crush	High Alert	Confused Names	Beers Criteria
No	No	Do not chew or open capsules	No	No	No

Drug Interactions: Simeprevir

Typical Agents	Mechanism	Clinical Management
P-glycoprotein inhibitors	Decreased simeprevir transport increases risk of simeprevir toxicity	Monitor carefully and consider simeprevir dose reduction
P-glycoprotein inducers	Increased simeprevir transport decreases simeprevir eff cacy	Avoid concurrent use, or monitor carefully and consider simeprevir dose increases
CYP3A4/5 inhibitors	Decreased simeprevir metabolism and increased risk of simeprevir toxicity	Avoid concurrent use or consider dose increases of simeprevir
CYP3A4/5 inducers	Increased simeprevir metabolism and decreased simeprevir eff cacy	Avoid concurrent use or consider dose decreases of simeprevir

Adverse Reactions: Simeprevir

Common (>10%)	Less Common (1-10%)	Rare but Serious (<1%)
Fatigue, headache, dizziness, insomnia, pruritus, rash, nausea, diarrhea, increased bilirubin, myalgia, dyspnea	Photosensitivity	None

Efficacy Monitoring Parameters. Improvement in signs and symptoms of hepatitis C infection. Monitor LFTs. Serum hepatitis C viral RNA levels prior and during treatment.

Toxicity Monitoring Parameters. In female patients and female partners of male patients, pregnancy tests should be done prior to and during treatment.

Key Patient Counseling Points. Must be taken in combination with other antiviral products, cannot be taken alone. Pregnancy warnings (due to ribavirin risk) for female patients and female partners of male patients. Avoid excessive sunlight and take precautions if exposed to sun. Take particular caution in patients of East Asian descent (higher risk of phototoxicity and rash).

Clinical Pearls. Astronomically expensive (approximately $80,000 per 12-wk course of therapy). Genetic category of HCV virus must be considered to determine appropriateness of treatment. Complicated stopping rules utilizing serum hepatitis C viral RNA levels (viral loads) used to determine overall length of treatment. Not recommended in patients who have failed simeprevir or other HCV protease inhibitor therapy in the past. Off-label dosing regimen for treatment of patients with HCV genotype 1 and 4 available.