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.

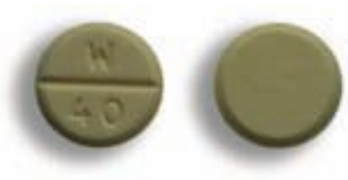
Key Patient Counseling Points. May cause drowsiness; avoid driving and operating heavy equipment. Heat prostration (due to decreased sweating) can occur when used in a hot environment.

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

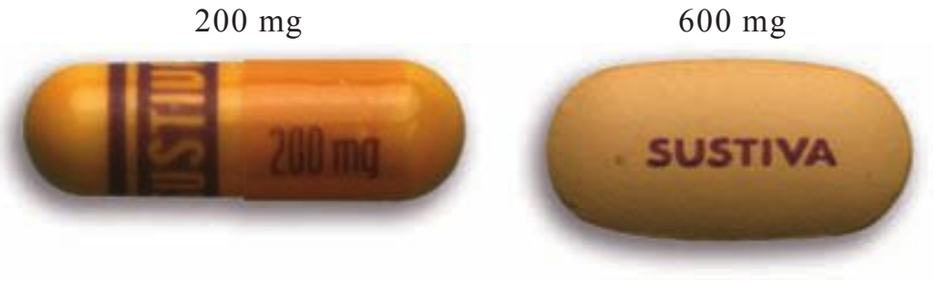
Dosage Forms. Oral Capsule: 50 mg, 200 mg; **Oral Tablet:** 600 mg

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

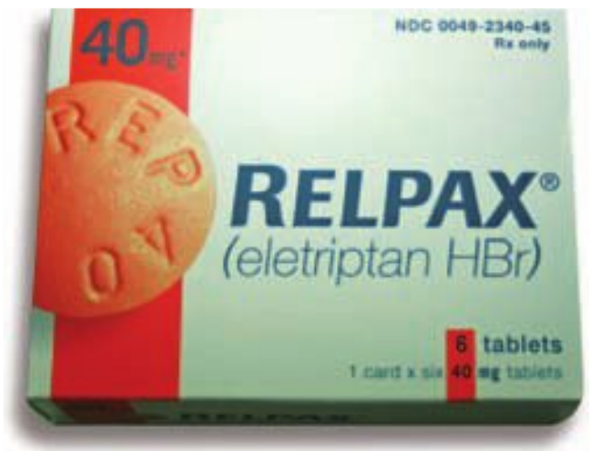
Dosage Forms. Oral Tablet: 20 mg, 40 mg

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

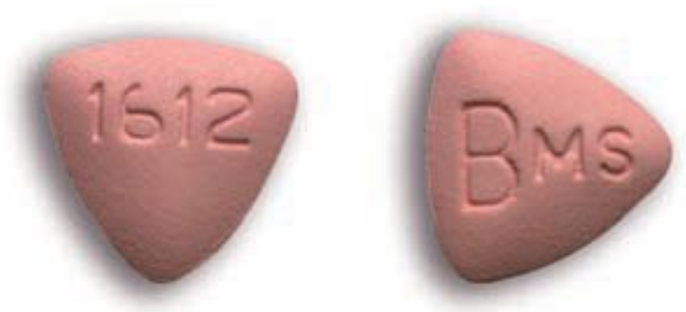
Common FDA Label Indication, Dosing, and Titration.

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.

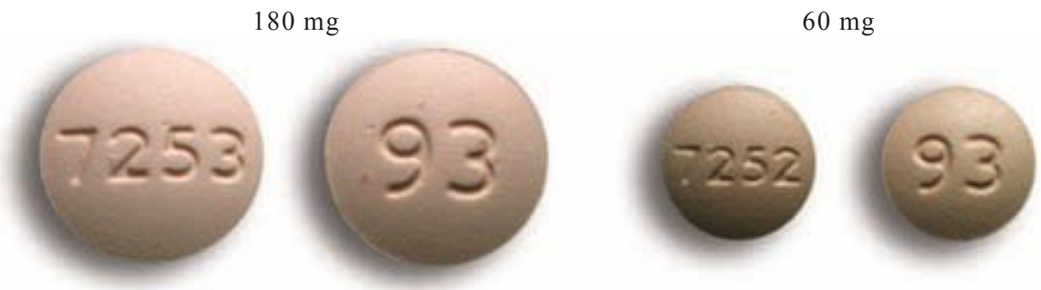
Key Patient Counseling Points. Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Apply to clean, dry skin. Skin breaks may increase absorption. Remove old patch when 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

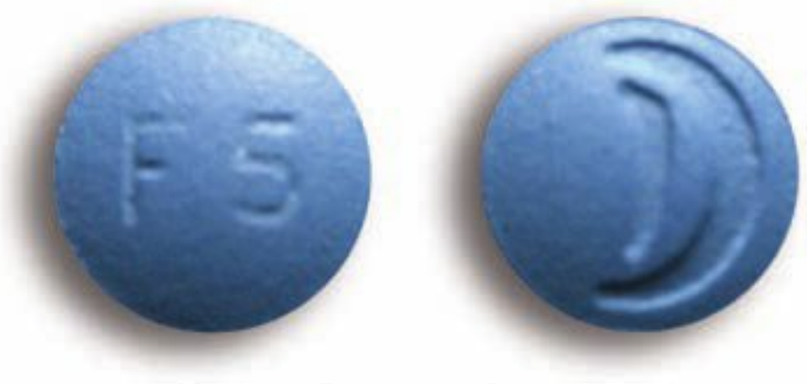
Common FDA Label Indication, Dosing, and Titration.

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.

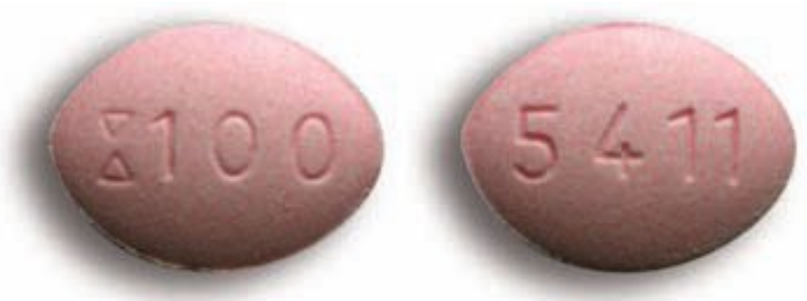
Key Patient Counseling Points. For hair loss, you may need to take this medicine for 3 mo or longer before you see an effect. For an enlarged prostate, you may need to take this medicine for up to 6 mo to see the full effect. Women who are pregnant or may become pregnant should avoid touching or handling 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

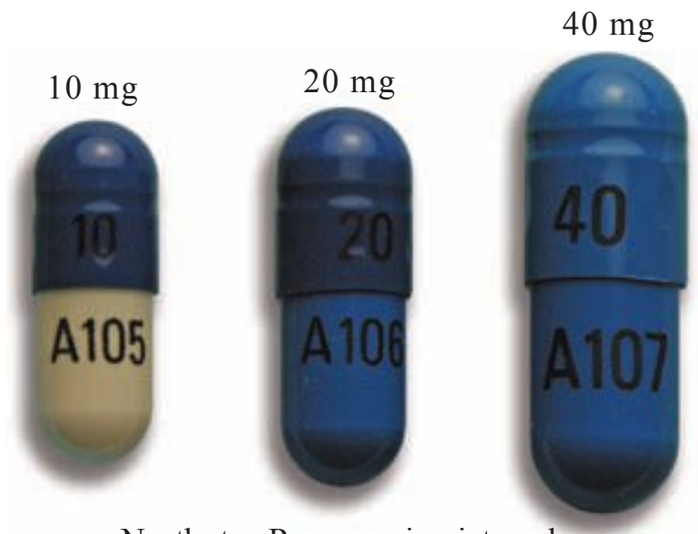
Dosage Forms. **Oral Capsule:** 10 mg, 20 mg, 40 mg; **Oral Capsule, Delayed Release, Weekly:** 90 mg; **Oral Tablet:** 10 mg, 20 mg, 60 mg; **Oral Solution, Oral Syrup:** 20 mg/5 mL

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.

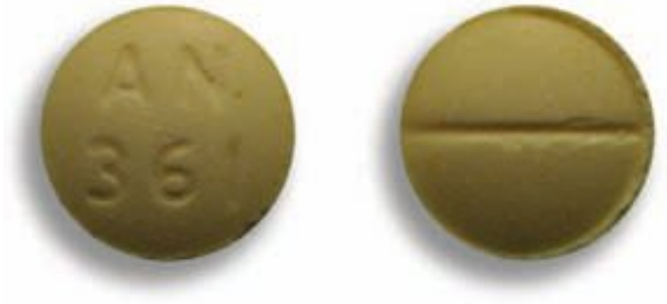
FOLIC ACID: Folacin-800, Various

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

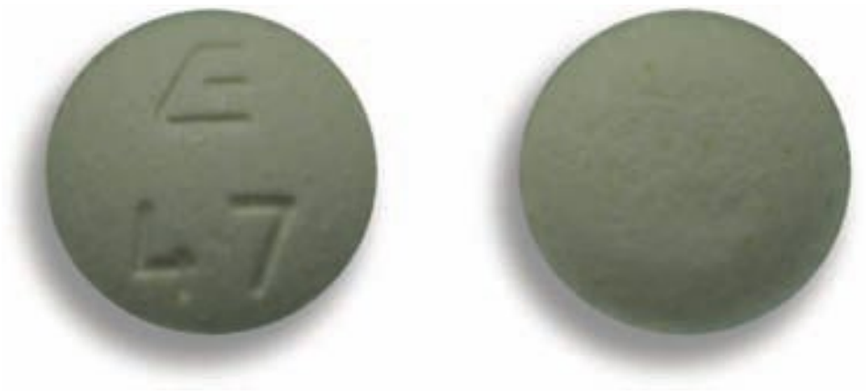
Dosage Forms. Oral Tablet: 10 mg, 20 mg, 40 mg

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.