Albumin (trade name®)

Scope CCT

Generic Name:	**Albumin**
Trade Name:	
Chemical Class:	Blood products,colloids
Therapeutic Class:	Volume expanders
Actions:	• Provides colloidal oncotic pressure, which serves to mobilize fluid from extravascular tissues back into the intravascular space. • Requires concurrent administration of appropriate crystalloid. **Therapeutic Effect(s):** Increase in intravascular fluid volume.
Pharmacokinetics:	**Absorption:** Following IV administration, absorption is essentially complete. **Distribution:** Confined to the intravascular space, unless capillary permeability is increased. **Metabolism and Excretion:** Probably degraded by the liver. **Half-life:** 2–3 wk. **TIME/ACTION PROFILE (oncotic effect)**

ROUTE	ONSET	PEAK	DURATION
IV	15–30 min	unknown	24 hr

Indications:	• Expansion of plasma volume and maintenance of cardiac output in situations associated with fluid volume deficit, including shock, hemorrhage, and burns. • Temporary replacement of albumin in diseases associated with low levels of plasma proteins, such as nephrotic syndrome or end-stage liver disease, resulting in relief or reduction of associated edema.
Contraindications/ Considerations:	**Contraindicated in:** • Allergic reactions to albumin; • Severe anemia; • HF; • Normal or increased intravascular volume. **Use Cautiously in:** • Severe hepatic or renal disease; • Dehydration (additional fluids may be required); • Patients requiring sodium restriction; • Preterm neonates (infuse slowly due to increased risk of intravascular hemorrhage).

Precautions:

- **Hepatic Impairment**
  Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
- **Renal Impairment**
  Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Pregnancy Cat: **Albumin** is classified as FDA pregnancy risk category C

Side Effects:

CNS: headache
CV: PULMONARY EDEMA, fluid overload, hypertension, hypotension, tachycardia
GI: increased salivation, nausea, vomiting
Derm: rash, urticaria
MS: back pain
Misc: chills, fever, flushing

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Hypovolemic shock–5% Albumin

IV: (Adults) 25 g (500 mL), may be repeated within 30 min.

IV: Children 0.5–1 g/kg/dose (10–20 mL/kg/dose) may repeat as needed (maximum 6 g/kg/day).

IV: (Infants and Neonates): 0.25–0.5 g/kg/dose (5–10 mL/kg/dose).

Supply: **Injection:** 5% (50 mg/mL), 25% (250 mg/mL)

Notes:

- Hemorrhage: Monitor hemoglobin and hematocrit levels. These values may ↓ because of hemodilution.
- Follow manufacturer's recommendations for administration. Administer through a large-gauge (at least 20-gauge) needle or catheter. Record lot number in patient record.
    - Solution should be clear amber; 25% albumin solution is equal to 5 times the osmotic value of plasma. Do not administer solutions that are discolored or contain particulate matter. Each L of both 5% and 25% albumin contains 130–160 mEq of sodium and is thus no longer labeled "salt-poor" albumin.
    - Administration of large quantities of normal serum albumin may need to be supplemented with whole blood to prevent anemia. If more than 1000 mL of 5% normal serum albumin is given or if hemorrhage has occurred, the administration of whole blood or packed RBCs may be needed. Hydration status should be monitored and maintained with additional fluids.
- **Intermittent Infusion: Diluent:** Administer 5% normal serum albumin undiluted. Normal serum albumin 25% may be administered undiluted or diluted in 0.9% NaCl, D5W, or sodium lactate injection; do not dilute in sterile water (may result in hypotonic-associated hemolysis which may be fatal). Infusion must be completed within 4 hr. **Concentration:** 5%: 50 mg/mL undiluted. 25%: 250 mg/mL undiluted.
- **Rate:** Rate of administration is determined by concentration of solution, blood volume, indication, and patient response (usual rate over 30–60 min). In patients with normal blood volume, rate of 5% and 25% solutions should not exceed 2–4 mL/min and 1 mL/min, respectively, for both adults and children.
    - **Hypovolemia:** 5% or 25% normal serum albumin may be administered as rapidly as tolerated and repeated in 15–30 min if necessary.
    - **Burns:** Rate after the first 24 hr should be set to maintain a plasma albumin level of 2.5 g/100 mL or a total serum protein level of 5.2 g/100 mL.

Bumetidine (Bumex®)

Scope CCT

Generic Name:	**Bumetidine**
Trade Name:	Bumex®
Chemical Class:	Loop Diuretic
Therapeutic Class:	Diuretic
Actions:	Inhibits the reabsorption of sodium and chloride from the loop of Henle and distal renal tubule. • Increases renal excretion of water, sodium chloride, magnesium, potassium, and calcium. • Effectiveness persists in impaired renal function.

Therapeutic Effect(s):
Diuresis and subsequent mobilization of excess fluid (edema, pleural effusions).

Pharmacokinetics:

Absorption: Well absorbed after oral or IM administration.

Distribution: Widely distributed.

Protein Binding: 72–96%.

Metabolism and Excretion: Partially metabolized by liver; 50% eliminated unchanged by kidneys and 20% excreted in feces.

Half-life: 60–90 min (6 hr in neonates).

TIME/ACTION PROFILE (diuretic effect)

ROUTE	ONSET	PEAK	DURATION
PO	30–60 min	1–2 hr	4–6 hr
IM	30–60 min	1–2 hr	4–6 hr
IV	2–3min	15–45 min	2–3 hr

Indications: Moderate to severe hypertension

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity;
- Cross-sensitivity with thiazides and sulfonamides may occur;
- Hepatic coma or anuria.

Use Cautiously in:

- Severe liver disease (may precipitate hepatic coma; concurrent use with potassium-sparing diuretics may be necessary);
- Electrolyte depletion;
- Diabetes mellitus;
- Increasing azotemia;
- Lactation: Pedi: Safety not established; bumetanide is a potent displacer of bilirubin and should be used cautiously in critically ill or jaundiced neonates because of risk of kernicterus. Injection contains benzyl alcohol, which may cause gasping syndrome in neonates;
- Geri: May have ↑ risk of side effects, especially hypotension and electrolyte imbalance, at usual doses

Precautions:

Hepatic Impairment: No specific dosage adjustment is needed in patients with hepatic impairment; see dosage for the treatment of ascites. In general, diuretics should be used with caution in patients with hepatic disease since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Renal Impairment : No specific dosage adjustments are recommended. Higher doses with extended dosage intervals may be effective in patients with end-stage renal disease (ESRD).

Pregnancy Cat:

Bumetadine is classified as FDA pregnancy risk category C

Side Effects:

- **CNS:** dizziness, encephalopathy, headache
- **EENT:** hearing loss, tinnitus
- **CV:** hypotension
- **GI:** diarrhea, dry mouth, nausea, vomiting
- **GU:** ↑ BUN, excessive urination
- **Derm:** STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, photosensitivity, pruritis, rash
- **Endo:** hyperglycemia, hyperuricemia
- **F and E:** dehydration, hypocalcemia, hypochloremia, hypokalemia, hypomagnesemia, hyponatremia, hypovolemia, metabolic alkalosis
- **MS:** arthralgia, muscle cramps, myalgia

* CAPITALS indicate life-threatening.
Underline indicate most frequent.

Administration:

IM: IV: (Adults) 0.5–1 mg/dose, may repeat q 2–3 hr as needed (up to 10 mg/day).

IM: IV: (Infants and Children): 0.015–0.1 mg/kg/dose every 6–24 hrs (maximum: 10 mg/day).

IM: IV: Neonates 0.01–0.05 mg/kg/dose every 12–24 in term neonates or every 24–48 hrs in preterm neonates.

Supply:

Bumetanide Intramuscular Inj Sol: 0.25mg, 1mL
Bumetanide Intravenous Inj Sol: 0.25mg, 1mL

Notes:

- ***BOXED WARNING***: **Anuria, dehydration, hypovolemia, oliguria, renal disease, renal failure, renal impairment**. Bumetanide can cause dehydration; the dehydration can be profound if bumetanide is given in excessive doses. Patients should be carefully monitored; dosage adjustments may be necessary. Because of this, bumetanide is contraindicated in any patient with anuria. Bumetanide should be used with caution in patients with severe renal disease such as severe renal impairment or renal failure. Bumetanide-induced hypovolemia can precipitate oliguria and azotemia in these patients. Although bumetanide can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or serum creatinine, or the development of oliguria

during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment with bumetanide. Renal failure may reduce drug clearance and warrant the use of higher doses with extended dosing intervals. Bumetanide may be less effective in patients with renal failure and higher doses may be required. Delayed excretion of bumetanide in patients with renal failure may increase the risk of toxicity (e.g., ototoxicity).

- •↑ risk of hypotension with antihypertensives , nitrates , or acute ingestion of alcohol .
- •↑ risk of hypokalemia with other diuretics , amphotericin B , stimulant laxatives , and corticosteroids .
- •Hypokalemia may ↑ risk of digoxin toxicity.
- •↓ lithium excretion, may cause lithium toxicity.
- •↑ risk of ototoxicity with aminoglycosides .
- • NSAIDS ↓ effects of bumetanide.
- **IV Push: Diluent:** Administer undiluted. **Concentration:** 0.25 mg/mL.
- **Rate:** Administer slowly over 1–2 min.
- **Continuous Infusion: Diluent:** May dilute in D5W or 0.9% NaCl. May also administer as undiluted drug. Protect from light. **Concentration:** Not to exceed 0.25 mg/mL.
- **Rate:** Infuse over 5 min. May be administered over 12 hr for patients with renal impairment.
-

Butorphanol (Stadol®)

Scope CCT

Generic Name:	**Butorphanol**
Trade Name:	**Stadol®**
Chemical Class:	Mixed Opioid agonists-antagonists
Therapeutic Class:	Opioid analgesics
Actions:	• Binds to opiate receptors in the CNS. • Alters the perception of and response to painful stimuli while producing generalized CNS depression. • Has partial antagonist properties that may result in opioid withdrawal in physically dependent patients. **Therapeutic Effect(s):** Decreased severity of pain.
Pharmacokinetics:	**Absorption:** Well absorbed from IM sites and nasal mucosa. **Distribution:** Crosses the placenta and enters breast milk. **Metabolism and Excretion:** Mostly metabolized by the liver; 11–14% excreted in the feces. Minimal renal excretion. **Half-life:** 3–4 hr. **TIME/ACTION PROFILE (analgesia)**

ROUTE	ONSET	PEAK	DURATION
IM	within 15 min	30–60 min	3–4 hr
IV	within mins	4–5 min	2–4 hr
Intranasal	within 15 min	1–2 hr	4–5 hr

Indications:

- Management of moderate to severe pain.
- Analgesia during labor.
- Sedation before surgery.
- Supplement in balanced anesthesia

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity;
- Patients physically dependent on opioids (may precipitate withdrawal).

Use Cautiously in:

- Head trauma;
- ↑ intracranial pressure;
- Severe renal, hepatic, or pulmonary disease (↑ interval to q 6–8 hr initially in hepatic/renal impairment);
- Hypothyroidism;
- Adrenal insufficiency;
- Alcoholism;
- Undiagnosed abdominal pain;
- Prostatic hyperplasia;
- OB: Lactation: Pedi: Safety not established but has been used during labor (may cause respiratory depression in the newborn);
- Geri: ↓ usual dose by 50%; give at twice the usual interval initially.

Precautions:

- **Hepatic Impairment**
  Intranasal dosage should not exceed 1 mg followed by 1 mg in 90—120 minutes. The initial IM or IV dose for pain relief should generally be half the recommended adult dose (0.5 mg IV or 1 mg IM). Repeat dosage interval for intranasal, IV, or IM administration should generally not be less than 6 hours.
- **Renal Impairment**
  Intranasal dosage should not exceed 1 mg followed by 1 mg in 90—120 minutes. The initial IM or IV dose for pain relief should generally be half the recommended adult dose (0.5 mg IV or 1 mg IM). Repeat dosage interval for intranasal, IV, or IM administration should generally not be less than 6 hours.

Pregnancy Cat: **Butorphanol** is classified as FDA pregnancy risk category C

Side Effects:

CNS: *confusion*, *dysphoria*, *hallucinations*, *sedation*, euphoria, floating feeling, headache, unusual dreams
EENT: blurred vision, diplopia, miosis (high doses)
Resp: respiratory depression
CV: hypertension, hypotension, palpitations
GI: *nausea*, constipation, dry mouth, ileus, vomiting
GU: urinary retention
Derm: *sweating*, clammy feeling
Misc: physical dependence, psychological dependence, tolerance
* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

IM: (Adults) 2 mg q 3–4 hr as needed (range 1–4 mg).

IV: (Adults) 1 mg q 3–4 hr as needed (range 0.5–2 mg).

IM: IV: Geriatric Patients 1 mg q 4–6 hr, ↑ as necessary.

Intranasal: (Adults) 1 mg (1 spray in 1 nostril) initially. An additional dose may be given 60–90 min later. This sequence may be repeated in 3–4 hr. If pain is severe, an initial dose of 2 mg (1 spray in each nostril) may be given. May be repeated in 3–4 hr.

Intranasal: Geriatric Patients 1 mg (1 spray in 1 nostril) initially. An additional dose may be given 90–120 min later. This sequence may be repeated in 3–4 hr.

Supply:

Injection: 1 mg/mL, 2 mg/mL
Intranasal solution: 10 mg/mL, in 2.5-mL metered-dose spray pump (14–15 doses; 1 mg/spray)

Notes:

- **High Alert Medication:** This medication bears a heightened risk of causing significant patient harm when it is used in error.
- **High Alert:** Accidental overdosage of opioid analgesics has resulted in fatalities. Before administering, clarify all ambiguous orders; have second practitioner independently check original order, dose calculations, route of administration, and infusion pump programming.
- Explain therapeutic value of medication before administration to enhance the analgesic effect.
- Regularly administered doses may be more effective than prn administration. Analgesic is more effective if given before pain becomes severe.
- Coadministration with nonopioid analgesics may have additive analgesic effects and permit lower opioid doses.
- **IM:** Administer IM injections deep into well-developed muscle. Rotate sites of injections.
- **Intranasal:** Administer 1 spray in 1 nostril.
- **IV Administration**
- **IV Push: Diluent:** May give IV undiluted.

- **Concentration:** 1–2 mg/mL.
- **Rate:** Administer over 3–5 min. **High Alert:** Rapid administration may cause respiratory depression, hypotension, and cardiac arrest.

Calcium Chloride 10%/Calcium Gluconate

Scope CCT

Generic Name:	**Calcium Chloride, Calcium Gluconate**
Trade Name:	Calcitrate, Calphron
Chemical Class:	Calcium Salt
Therapeutic Class:	Electrolyte supplement, Parenteral
Actions:	Calcium chloride is more bioavailable than calcium gluconate and results in greater increases in serum ionized calcium concentrations than does calcium gluconate.
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ =. Calcium is 40% bound to plasma proteins, primarily albumin, and 10% is in a chelated form. Approximately 50% of serum calcium is ionized, which is considered the physiologically active form However, approximately 99% of filtered calcium is reabsorbed by the kidney with less than 1% excreted. Parathyroid hormone, calcitonin, and 1,25 dihydroxycholecalciferol are primarily responsible for controlling calcium equilibrium. Insulin, thyroxine, growth hormone, androgens, estrogens, adrenal corticosteroids, and inorganic phosphate also contribute.
Indications:	• Ionized Hypocalcemia, Hyperkalemia, Hypermagnesemia,
Contraindications:	• **Extravasation, intramuscular administration, subcutaneous administration**
Precautions:	**Hyperphosphatemia, hypoparathyroidism** Calcium supplements should be used with caution in patients with chronic renal failure due to the increased risk of developing hypercalcemia.
Pregnancy Cat.	FDA pregnancy risk category C
Side Effects:	**Severe** tissue necrosis, AV block, cardiac arrest, coma, bradycardia ventricular fibrillation , milk-alkali syndrome
Administration:	**Intravenous Administration** **Other Injectable Administration** **Intraosseous Route** **NOTE: Calcium chloride and calcium gluconate are not approved by the FDA for intraosseous administration.**

During cardiopulmonary resuscitation in pediatrics, calcium chloride or calcium gluconate may be given via the intraosseous route when IV access is not available.

Adult

Acute Hypocalcemia
1 g IV slowly at a rate not exceeding 1 ml/min.

Hypocalcemia secondary to multiple citrated blood transfusions
Administer 500 mg IV slowly at a rate not exceeding 1 ml/min.

Hypermagnesemia
(for patients on Magnesium drip who show s/s of toxicity or known hypermagnesemia by labs): mix 500mg in 100 ml and infuse over 15 minutes.

Betablocker Overdose
1 gm over 5 minutes. Call for additional doses.

IV Push
In general, inject IV 10% calcium gluconate products slowly, at a rate of 1.5 mL/minute (150 mg/minute) or less to avoid adverse reactions. The absolute maximum rate of 2 mL/minute (200 mg/minute) should not be exceeded.
Administer through a small needle into a large vein.
Inject IV 10% calcium chloride by slow IV injection. Do not to exceed 1 mL/minute (100 mg/minute), preferably in a deep or central vein.

Intermittent IV Infusion
May dilute in compatible IV solution (i.e., 0.9% Sodium Chloride injection, 5% Dextrose injection, 10% Dextrose injection) to a usual concentration of 10 to 40 mg/mL.

Pediatric

Do not administer via scalp vein catheter.
Intraosseous Route
NOTE: Calcium chloride and calcium gluconate are not approved by the FDA for intraosseous administration.
During cardiopulmonary resuscitation in pediatrics, calcium chloride or calcium gluconate may be given via the intraosseous route when IV access is not available.

Supply: Calcium/Calcium Chloride/Calcium Gluconate Intravenous Inj Sol: 1mL, 10%, 100mg

Notes: For Calcium Chloride administration, a large central vein is preferred for administration.

Hepatic Impairment
Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
Renal Impairment

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Interactions

Succinylcholine: (Moderate) Calcium salts may antagonize the effects of nondepolarizing neuromuscular blockers.

Vecuronium: (Moderate) Calcium salts may antagonize the effects of nondepolarizing neuromuscular blockers.

Scope CCT

Generic Name:	**Captopril**
Trade Name:	Capoten®
Chemical Class:	Ace Inhibitor
Therapeutic Class:	Antihypertensive
Actions:	Captopril has a high affinity for ACE and competes with angiotensin I, the natural substrate, to block its conversion to angiotensin II. Angiotensin II is a potent vasoconstrictor and a negative feedback mediator for renin activity. Thus, as a result of lower angiotensin II plasma levels, blood pressure decreases and plasma renin activity increases. In addition, baroreceptor reflex mechanisms are stimulated by the drop in blood pressure. Kininase II, identical to ACE, is an enzyme that degrades bradykinin, a potent vasodilator, to inactive peptides. Whether increased bradykinin levels play a part in the therapeutic effects of ACE inhibitors is presently unclear. Bradykinin-induced vasodilation is thought to be of secondary importance in the blood-pressure lowering effect of ACE inhibitors. A bradykinin mechanism may, however, contribute to ACE-inhibitor-induced angioneurotic edema and cough. The "local" activity of ACE inhibitors may be more responsible for their clinical effects than systemic activity. ACE-inhibiting drugs may act locally (i.e., within a specific tissue) to reduce vascular tone by decreasing local angiotensin II-induced sympathetic activity and/or by decreasing local angiotensin II-induced vasoconstrictive activity. ACE inhibitors may inhibit presynaptic norepinephrine release and postsynaptic adrenergic receptor activity, decreasing vascular sensitivity to vasopressor activity. Decreases in plasma angiotensin II levels reduce aldosterone secretion, with a subsequent decrease in sodium and water retention. Captopril dilates arterioles, thereby lowering total peripheral vascular resistance. In hypertensive patients, blood pressure is decreased with little or no change in heart rate, stroke volume, or cardiac output. However, captopril can increase cardiac output, cardiac index, stroke volume, and exercise tolerance in patients with congestive heart failure. The drug also decreases pulmonary wedge pressure, pulmonary vascular resistance, and mean arterial and right atrial pressures in these patients. As antihypertensives, ACE inhibitors reduce LVH, do not worsen insulin resistance or hyperlipidemia, and do not cause sexual dysfunction.
Pharmacokinetics:	**Absorption: 60–75% absorbed following oral administration (decreased by food).** **Distribution: Crosses the placenta; enters breast milk in small amounts.**

Metabolism and Excretion: 50% metabolized by the liver to inactive compounds, 50% excreted unchanged in urine.

Half-life: Infants with HF: 3.3 hr (range 1.2–12.4 hr); Children: 1.5 hr (range 0.98–2.3 hr); Adults: 1.9 hr (↑ to 20–40 hr in renal impairment); Adults with HF: 2.1 hr.

TIME/ACTION PROFILE (effect on BP–single dose†)

ROUTE	ONSET	PEAK	DURATION
PO	15–60 min	60–90 min	6–12 hr

†Full effects may not be noted for several weeks.

Indications:

- Alone or with other agents in the management of hypertension.
- Management of heart failure.
- Reduction of risk of death, heart failure-related hospitalizations, and development of overt heart failure following myocardial infarction.
- Treatment of diabetic nephropathy in patients with Type 1 diabetes mellitus and retinopathy.

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity
- History of angioedema with previous use of ACE inhibitors
- Concurrent use with aliskiren in patients with diabetes or moderate-to-severe renal impairment (CCr <60 mL/min);
- OB: Can cause injury or death of fetus – if pregnancy occurs, discontinue immediately
- Lactation: Discontinue drug or use formula.

Use Cautiously in:

- Patients with collagen vascular disease, renal impairment, hypovolemia, hyponatremia, and concurrent diuretic therapy
- Surgery/anesthesia (hypotension may be exaggerated)
- Black patients (monotherapy for hypertension less effective, may require additional therapy; higher risk of angioedema)
- Women of childbearing potential
- Geri: Initial dose ↓ recommended.

Exercise Extreme Caution in:

History of angioedema**.**

Precautions:

Hepatic Impairment

No dosage adjustments are recommended for captopril in hepatic impairment**.**

Renal Impairment

CrCl more than 50 mL/minute: no dosage adjustment needed.

CrCl 10 to 50 mL/minute: reduce recommended dose by 25%.

CrCl less than 10 mL/minute: reduce recommended dose by 50%.

Intermittent hemodialysis

Captopril is significantly removed by dialysis; doses should be given after dialysis. For pediatric patients, an initial dose reduction of 50% is recommended. Evaluate and adjust dosage of captopril based on clinical response to therapy.

Peritoneal dialysis

Adult patients: Reduce the initial dose by 25%, then titrate to desired clinical effect.

Pediatric patients: Reduce the initial dose by 50%, then titrate to desired clinical effect.

Continuous renal replacement therapy (CRRT)

Reduce the initial dose by 25%, then titrate to desired clinical effect.

Pregnancy Cat:

Captopril is classified as FDA pregnancy risk category D

Side Effects:

Severe:

- peptic ulcer
- hepatic failure
- hepatic necrosis
- heart failure
- myocardial infarction
- oliguria
- nephrotic syndrome
- renal failure (unspecified)
- hemolytic anemia
- aplastic anemia
- pancytopenia
- agranulocytosis
- cardiac arrest
- arrhythmia exacerbation
- eosinophilic pneumonia
- bronchospasm
- vasculitis
- Stevens-Johnson syndrome
- erythema multiforme
- exfoliative dermatitis
- angioedema
- anaphylactoid reactions
- hyperkalemia
- pancreatitis
- teratogenesis

Moderate

- constipation
- dyspnea
- proteinuria
- palpitations
- chest pain (unspecified)

- sinus tachycardia
- angina
- thrombocytopenia
- neutropenia
- anemia
- glossitis
- orthostatic hypotension
- hypotension
- eosinophilia
- hepatitis
- elevated hepatic enzymes
- cholestasis
- jaundice
- hyponatremia
- ataxia
- depression
- confusion
- blurred vision
- myasthenia

Administration:

Oral Administration

To ensure maximum absorption, administer on an empty stomach 1 hour before meals. Drug absorption is reduced 30—40% by food.

For the treatment of hypertension.

Oral dosage

Adults

Initially, 12.5—25 mg PO, given 2—3 times per day. May increase to 50 mg PO three times daily after 1—2 weeks if needed. A diuretic may be added after 1—2 weeks if needed. If patient is already receiving a diuretic, lower initial doses should be used. Maintenance dosage range is 25—150 mg PO 2—3 times per day. The maximum daily dose is 150 mg three times per day; this daily dose of 450 mg may also be given in 2 divided doses per day. Most clinicians recognize 150 mg/day as the effective maximum daily dose, above which adverse reactions increase.

Geriatric

Initiate therapy at the lower end of the adult dosage range. Greater sensitivity to the usual adult dose is possible. Adjust dosage based on clinical response.

Children† and Adolescents†

Initially, 0.3—0.5 mg/kg PO per dose. Maximum dosage is 6 mg/kg/day, given in 2—4 divided doses. Although a specific total mg maximum dose has not been clearly defined, initial and final doses should not exceed those recommended for adult patients (e.g. 12.5—25 mg/dose for initial doses and 450 mg/day for the final dose).

Infants†

Initially, 0.15—0.3 mg/kg PO per dose. Maximum dosage is 6 mg/kg/day, given in 1—4 divided doses. The usual dosage is 2.5—6 mg/kg/day.

Neonates†

Initially, 0.01—0.1 mg/kg/dose PO every 8—24 hours. Titrate dose up based on clinical response to 0.5 mg/kg/dose PO every 6—24 hours.

For the treatment of heart failure.

Oral dosage

Adults

Initially, 6.25 mg PO 3 times daily. Clinical practice guidelines suggest titration to a maximum dose of 50 mg PO 3 times daily. The maximum daily dose recommended by the manufacturer is 450 mg/day, although **most** patients will see satisfactory clinical improvement at 50 to 100 mg 3 times daily. When possible, further increases in dosages above 50 mg PO 3 times daily should be delayed for at least 2 weeks to determine is satisfactory response occurs. To reduce morbidity and mortality associated with heart failure, clinical practice guidelines recommend treatment with angiotensin converting enzyme (ACE) inhibitors for all patients with current or prior symptoms of heart failure and reduced left ventricular ejection fraction, unless contraindicated. ACE inhibitors also should be used to prevent symptomatic heart failure and reduce mortality in all patients with a reduced ejection fraction with or without a recent or remote history of myocardial infarction or acute coronary syndrome.

Adolescents†

Some experts recommend initial doses of 6.25 to 12.5 mg PO every 8 to 12 hours titrated up as needed to a maximum of 50 to 75 mg/dose.

Children†

Some experts recommend a dosage range of 0.1 to 2 mg/kg/dose PO every 6 to 12 hours, not to exceed a total daily dose of 6 mg/kg/day. NOTE: Initial doses (e.g. 0.1 mg/kg/dose) are often lower than the initial doses used for hypertension. Although a specific total mg maximum dose has not been clearly defined, initial and final doses should not exceed those recommended for adult patients (e.g. 12.5 to 25 mg/dose for initial doses and 150 mg/day for the final dose).

Infants†

Initially, 0.15 to 0.3 mg/kg PO per dose. The usual required dose is 2.5 to 6 mg/kg/day. Maximum dosage is 6 mg/kg/day PO, given in 1 to 4 divided doses.

Neonates†

Initially, 0.05 to 0.1 mg/kg PO every 8 to 24 hours, titrate up to 0.5 mg/kg PO every 6 to 24 hours. Do not exceed 2 mg/kg/day.

Premature Neonates†

Initially, 0.01 mg/kg PO every 8 to 12 hours.

For the treatment of hypertensive urgency† or hypertensive emergency†.

Oral dosage

Adults

25 mg PO, may repeat every 30 minutes as needed.

Geriatric

Initiate therapy at the lower end of the adult dosage range. Greater sensitivity to the usual adult dose is possible. Adjust dosage based on clinical response.

For the treatment of acute myocardial infarction† or postmyocardial infarction.

In patients with left ventricular dysfunction (ejection fraction <= 40%).

Oral dosage

NOTE: The American College of Cardiology/American Heart Association guidelines recommend initiation of ACE inhibitor therapy within 24 hours of an evolving acute myocardial infarction in patients with ST segment elevation or LBBB, provided the patient does not have hypotension or other contraindication.

Adults

Doses of 6.25—12.5 mg PO three times daily, were initiated within 3—16 days in patients with asymptomatic left ventricular dysfunction after **acute** myocardial infarction. Doses were escalated gradually to 25 mg PO three times per day over the next several days. Over the next several weeks titration to a target dosage of 50 mg PO three times per day occurred. Patients were followed for an average of 42 months. Long-term administration of captopril was associated with an improvement in survival and a reduction in mortality and morbidity due to severe congestive heart failure or the recurrence of fatal or nonfatal myocardial infarction in this patient population.

Geriatric

Initiate therapy at the lower end of the adult dosage range. Greater sensitivity to the usual adult dose is possible. Adjust dosage based on clinical response.

In patients without left ventricular dysfunction†.

NOTE: The American College of Cardiology/American Heart Association guidelines recommend initiation of ACE inhibitor therapy within 24 hours of an evolving acute myocardial infarction in patients with ST segment elevation or LBBB, provided the patient does not have hypotension or other contraindication.

Oral dosage

Adults

The ISIS-4 study compared captopril, oral mononitrate, and IV magnesium sulfate as post-acute myocardial infarction interventions in 58,050 patients to assess an affect on mortality. Oral captopril, but not the other 2 regimens, significantly reduced 5-week mortality compared to placebo. The dose of captopril in the ISIS-4 study was 6.25 mg PO initially, followed 2 hours later with 12.5 mg PO, followed 10—12 hours later with 25 mg PO. Thereafter, and for a total of 28 days, patients received 50 mg PO twice daily. In patients without complications and no evidence of symptomatic or asymptomatic LV dysfunction by 6 weeks after myocardial infarction, ACE inhibitor therapy can be stopped.

Geriatric

Initiate therapy at the lower end of the adult dosage range. Greater sensitivity to the usual adult dose is possible. Adjust dosage based on clinical response.

†Indicates off-label use

Supply: Capoten/Captopril Oral Tab: 12.5mg, 25mg, 50mg, 100mg

Notes: ***BOXED WARNING***

Neonates, pregnancy

When used during human pregnancy during the second and third trimesters, captopril, like other angiotensin-converting enzyme (ACE) inhibitors, can cause injury and even death to the developing fetus. When pregnancy is detected, captopril should be discontinued as soon as possible. Women of child-bearing age should be made aware of the potential risk and ACE inhibitors should only be given after careful counseling and consideration of individual risks and benefits. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible and monitoring of the fetal development should be performed on a regular basis. Rarely (probably less often than once per every thousand pregnancies), no alternative to ACE inhibitors will be found. In these rare cases, the pregnant women should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment. The reported adverse fetal and neonatal effects (e.g., hypotension, neonatal skull hypoplasia and craniofacial deformation, fetal limb contractures, hypoplastic lung development, anuria, oligohydramnios, reversible or irreversible renal failure, and death) have been reported during ACE inhibitor exposure during the second and third trimesters. An observational study based on Tennessee Medicaid data reported that the risk of congenital malformations is significantly increased during first-trimester exposure to ACE inhibitors. However, a much larger observational study (n = 465,754) found that the risk of birth defects was similar in babies exposed to ACE inhibitors during the first trimester, in those exposed to other antihypertensives during the first trimester, and in those whose mothers were hypertensive but were not treated. Newborns born to mothers with hypertension, either treated or untreated, had a higher risk of birth defects than those born to mothers without hypertension. The authors concluded that the presence of hypertension likely contributed to the development of birth defects rather than the use of medications. Further evaluation of teratogenicity data associated with ACE inhibitor exposure during pregnancy is ongoing. Closely observe neonates with histories of in utero exposure to captopril for hypotension, oliguria, and hyperkalemia. If oliguria or hypotension occurs, blood pressure and renal perfusion support may be required, as well as exchange transfusion or dialysis to reverse hypotension and/or support decreased renal function.

- Excessive hypotension may occur with concurrent use of diuretics .
- Additive hypotension with other antihypertensives .
- ↑ risk of hyperkalemia with concurrent use of potassium supplements , potassium-sparing diuretics , or potassium-containing salt substitutes .
- ↑ risk of hyperkalemia, renal dysfunction, hypotension, and syncope with concurrent use of angiotensin II receptor blockers or aliskiren; avoid concurrent use with aliskiren in patients with diabetes or CCr <60 mL/min; avoid concurrent use with angiotensin II receptor blockers
- NSAIDs and selective COX-2 inhibitors may blunt the antihypertensive effect and ↑ the risk of renal dysfunction.
- ↑ levels and may ↑ the risk of lithium toxicity.
- ↑ risk of angioedema with temsirolimus , sirolimus , or everolimus .
- Avoid natural licorice (causes sodium and water retention and increases potassium loss).
- Food significantly ↓ absorption. Administer captopril 1 hr before meals

Cefazolin (Ancef®)

Scope CCT

Generic Name:	**Cefazolin**
Trade Name:	Ancef®
Chemical Class:	First Generation Cephalosporin
Therapeutic Class:	Anti-infective
Actions:	Cefazolin, a beta-lactam antibiotic similar to penicillins, inhibits the third and final stage of bacterial cell wall synthesis by preferentially binding to specific penicillin-binding proteins (PBPs) that are located inside the bacterial cell wall. Penicillin-binding proteins are responsible for several steps in the synthesis of the cell wall and are found in quantities of several hundred to several thousand molecules per bacterial cell. Penicillin-binding proteins vary among different bacterial species. Thus, the intrinsic activity of cefazolin as well as other cephalosporins and penicillins against a particular organism depends on their ability to gain access to and bind with the necessary PBP. Like all beta-lactam antibiotics, cefazolin's ability to interfere with PBP-mediated cell wall synthesis ultimately leads to cell lysis. Lysis is mediated by bacterial cell wall autolytic enzymes (i.e., autolysins). The relationship between PBPs and autolysins is unclear, but it is possible that the beta-lactam antibiotic interferes with an autolysin inhibitor.
Pharmacokinetics:	**Absorption:** Well absorbed after IM administration. **Distribution:** Widely distributed. Penetrates bone and synovial fluid well. Crosses the placenta and enters breast milk in low concentrations. Minimal CSF penetration. **Protein Binding:** 74–86%. **Metabolism and Excretion:** Excreted almost entirely unchanged by the kidneys. **Half-life:** Neonates: 3–5 hrs; Adults: 90–150 min (↑ in renal impairment). **TIME/ACTION PROFILE (blood levels)**

ROUTE	ONSET	PEAK	DURATION
IM	rapid	0.5–2 hr	6–12 hr
IV	rapid	5 min	6–12 hr

Indications:	For the treatment of upper respiratory tract infections, lower respiratory tract infections (e.g. pneumonia), skin and skin structure infections, bone and joint infections, bacteremia, and biliary tract infections caused by susceptible organisms**.**
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity to cephalosporins • Serious hypersensitivity to penicillins. **Use Cautiously in:** • Renal impairment (dose ↓ and/or ↑ dosing interval recommended if CCr <30 mL/min) • Hepatic impairment • History of GI disease, especially colitis • OB: Half-life is shorter and blood levels lower during pregnancy; has been used safely.Lactation: Low concentrations of drug appear in breast milk

- Geri: Dose adjustment due to age-related ↓ in renal function may be necessary.

Precautions:

Hepatic Impairment
Cefazolin is primarily eliminated by the kidneys and is not metabolized by the liver. No dosage adjustments are required in patients with hepatic impairment.
Renal Impairment
Adults:
CrCl > 54 mL/min: no dosage adjustment needed.
CrCl 35—54 mL/min: reduce frequency to at least every 8 hours.
CrCl 11—34 mL/min: after a loading dose, reduce maintenance dose by 50% and administer every 12 hours.
CrCl < 10 mL/min: after a loading dose, reduce the recommended dose by 50% and administer every 18—24 hours.

Children:
CrCl > 70 mL/min: no dosage adjustment needed.
CrCl 40—70 mL/min: after an initial loading dose, reduce maintenance dose to 7.5—30 mg/kg IM or IV and administer every 12 hours.
CrCl 20—39 mL/min: after an initial loading dose, reduce maintenance dose to 3.125—12.5 mg/kg IM or IV and administer every 12 hours.
CrCl 5—19 mL/min: after an initial loading dose, reduce maintenance dose to 2.5—10 mg/kg IM or IV and administer every 24 hours.

Pregnancy Cat:

Cefazolin is classified as FDA pregnancy risk category B

Side Effects:

Severe:

- interstitial nephritis
- serum sickness
- hemolytic anemia
- seizures
- anaphylactic shock
- anaphylactoid reactions
- azotemia
- renal failure (unspecified)
- toxic epidermal necrolysis
- angioedema
- erythema multiforme
- Stevens-Johnson syndrome
- acute generalized exanthematous pustulosis (AGEP)
- aplastic anemia
- pancytopenia
- agranulocytosis

Moderate:

- eosinophilia
- elevated hepatic enzymes
- thrombocytopenia
- hypoprothrombinemia

- neutropenia
- oral ulceration
- colitis
- leukopenia
- bleeding
- thrombocytosis
- phlebitis
- confusion
- hypotension
- cholestasis
- hepatitis
- pseudomembranous colitis
- vaginitis
- superinfection
- candidiasis
- hypertonia

Administration:

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

Reconstitution

Vials: Reconstitute powder with Sterile Water for Injection. Use 2 mL for 500 mg vial (resultant concentration = 225 mg/mL) and 2.5 mL for 1 g vial (resultant concentration = 330 mg/mL).

Dilution

Intermittent IV injection: Further dilute the reconstituted solution with Sterile Water for Injection to a maximum concentration of 100 mg/mL for direct injection.

Intermittent IV Injection

Inject IV over 3 to 5 minutes.

1gm

Supply: Ancef/Cefazolin/Cefazolin Sodium/Kefzol Intramuscular Inj Pwd F/Sol: 1g, 10g, 20g, 500mg
Ancef/Cefazolin/Cefazolin Sodium/Kefzol Intravenous Inj Pwd F/Sol: 1g, 2g, 10g, 20g, 500mg
Cefazolin Sodium, Dextrose/Cefazolin, Dextrose Intravenous Inj Sol: 20-4g

Notes:	• **Probenecid** ↓ excretion and ↑ blood levels of renally excreted cephalosporins

Cimetidine (Tagamet ®)

Scope CCT

Generic Name:	**Cimetidine**
Trade Name:	Tagamet
Chemical Class:	H2 receptor-antagonist
Therapeutic Class:	Proton Pump Inhibitor
Actions:	Selectively antagonizes histamine (H2) receptors
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ = 2 hours.
Indications:	• Anaphylaxis, GI bleed, GI prophylaxis
Contraindications:	• Hypersensitivity to drug, class or component.
Precautions:	• Caution in: renal impairment, hepatic impairment, immunocompromised, chronic pulmonary disease, diabetes mellitus or elderly patients.
Pregnancy Cat.	B
Side Effects:	neutropenia thrombocytopenia agranulocytosis aplastic anemia pneumonia depression psychosis hallucinations anaphylaxis/anaphylactoid reaction pancreatitis interstitial nephritis bradycardia tachycardia AV block skin reaction, severe

Administration: Dilute Cimetidine Injection, USP, 300 mg, in at least 50 mL of 5% Dextrose Injection, or another compatible I.V. solution

Adult 300 mg IV or IM every 6 to 8 hours

Supply: Single-dose Flip top Vial- each mL contains cimetidine hydrochloride equivalent to 150 mg cimetidine.

Notes:

- Consider administration for GI prophylaxis in intubated patients who have not received any proton pump inhibitors.
- Drug Interactions: Cimetidine, apparently through an effect on certain microsomal enzyme systems, has been reported to reduce the hepatic metabolism of warfarin-type anticoagulants, phenytoin, propranolol, nifedipine, chlordiazepoxide, diazepam, certain tricyclic antidepressants, lidocaine, theophylline and metronidazole, thereby delaying elimination and increasing blood levels of these drugs.
- Immunocompromised Patients: In immunocompromised patients, decreased gastric acidity, including that produced by acid-suppressing agents such as cimetidine, may increase the possibility of a hyperinfection of strongyloidiasis.

Diazepam (Valium®)

Scope CCT

Generic Name:	**Diazepam**
Trade Name:	Valium
Chemical Class:	Benzodiazepine
Therapeutic Class:	Sedative-hypnotic, anticonvulsant, anti-anxiety
Actions:	Exact sedative mechanism unknown. Suppresses spread of seizure activity across the motor cortex.
Pharmacokinetics:	Onset 1-5 min. Peak 15 min. Duration. $t_{½}$ =.
Indications:	• Status epilepticus, acute anxiety, premedication for painful procedures
Contraindications:	• Patients with hypersensitivity to the drug. Shock. Coma. Severe Hepatic Disease. **Boxed warning:** Asthma, COPD, coadministration with other CNS depressandt, pulmonary disease, respiratory depression, respiratory insufficiency, sleep apnea. As with other benzodiazepines, diazepam should be used with caution in patients with pulmonary disease. Additionally, avoid coadministration with other CNS depressants, especially opioids, unless no other alternatives are available as coadministration significantly increases the risk for respiratory depression, low blood pressure, and death. Diazepam should be used with caution in other pulmonary diseases as well including severe chronic obstructive pulmonary disease (COPD), sleep apnea, asthma, or pneumonia because the drug can exacerbate ventilatory failure. Lower doses are recommended in patients with chronic respiratory insufficiency.
Precautions: ***Pregnancy Cat.***	• Use IV diazepam with extreme caution in the elderly, the very ill, and patients with COPD • **Dilution may cause precipitation.** D
Side Effects:	Bradycardia Apnea Cardiac Arrest Seizures Teratogenesis Thrombosis Drowsiness Fatigue Confusion Dizziness Hypotension Tachycardia Blurred vision Nausea

	Respiratory depression Nystagmus
Administration:	IV, IM **Dilution may cause precipitation** Strict aseptic technique must always be maintained during handling of parenteral products. Diazepam injectable emulsion (Dizac) contains no antimicrobial preservatives and can support rapid growth of microorganisms. ***Adult*** *Seizures* 5 mg IV or IM, repeat up to max of 10 mg IV or IM *Anxiety* 2 mg IV repeat as ordered *Premedication* 5 mg IV repeat up to max dose of 15 mg IV *Pediatric*
Supply:	Diazepam/Dizac/Valium Intramuscular Inj Sol: 1mL, 5mg Diazepam/Dizac/Valium Intramuscular Sol: 1mL, 5mg Diazepam/Dizac/Valium Intravenous Inj Sol: 1mL, 5mg Diazepam/Dizac/Valium Intravenous Sol: 1mL, 5mg
Notes:	•

Dobutamine (Dobutrex®)

Scope CCT

Generic Name:	**Dobutamine**
Trade Name:	Dobutrex®
Chemical Class:	Adrenergic Agonist
Therapeutic Class:	Inotrope
Actions:	Dobutamine is a direct-acting sympathomimetic. It is primarily an agonist at beta1-adrenergic receptors, with minor beta2 and alpha1 stimulatory effects. Clinical actions reflect both beta agonism by the (+) isomer and the alpha agonism by the less potent (-) isomer. Agonism at the beta1-adrenergic receptor predominates and increases myocardial contractility and stroke volume with modest chronotropic effects, resulting in increased cardiac output. The inotropic effects are dose-dependent. Dobutamine's secondary hemodynamic effects include decreases in systemic vascular resistance (afterload) and ventricular filling pressure (preload). Systolic blood pressure is generally elevated as a consequence of increased stroke volume, although diastolic blood pressure and mean arterial pressure are usually unchanged with normal doses in normotensive patients. Increased myocardial contractility results in increased coronary blood flow and myocardial oxygen consumption. Dobutamine has minimal effect on pulmonary vascular resistance. Unlike dopamine, dobutamine does not affect dopaminergic receptors, nor does it cause release of norepinephrine from sympathetic nerve endings. Urinary output can increase, however, secondary to increased cardiac output. Electrophysiologically, dobutamine can facilitate AV nodal conduction, particularly in patients with concomitant atrial fibrillation.
Pharmacokinetics:	**Absorption:** Administered by IV infusion only, resulting in complete bioavailability. **Distribution:** Unknown. **Metabolism and Excretion:** Metabolized by the liver and other tissues. **Half-life:** 2 min. **TIME/ACTION PROFILE (inotropic effects)**

ROUTE	ONSET	PEAK	DURATION
IV	1–2 min	10 min	brief (min)

Indications:	Short term management of depressed cardiac output in patients with heart failure, management of sepsis-induced myocardial dysfunction
Contraindications/ Considerations:	**Contraindicated in:** Hypersensitivity to dobutamine or bisulfites;Idiopathic hypertrophic subaortic stenosis**.** **Use Cautiously in:** History of hypertension (increased risk of exaggerated pressor response); MI; Atrial fibrillation (pretreatment with digitalis glycosides recommended); History of ventricular atopic activity (may be exacerbated); Hypovolemia (correct before administration); Pregnancy or lactation (safety not established).

Precautions:

Hepatic Impairment
Specific guidelines for dosage adjustments are not available; it appears that no dosage adjustments are needed. Titrate the dobutamine infusion rate to attain clinical goals.

Renal Impairment
Specific guidelines for dosage adjustments are not available; it appears that no dosage adjustments are needed. Titrate the dobutamine infusion rate to attain clinical goals.

Intermittent hemodialysis
It is unknown whether dobutamine is dialyzable. Titrate the dobutamine infusion rate to attain clinical goals.

Pregnancy Cat: Dobutamine is classified as FDA pregnancy risk category B

Side Effects:

Severe:

- ventricular tachycardia,
- arrhythmia exacerbation
- pulmonary edema
- skin necrosis
- bronchospasm
- anaphylactoid reactions

Moderate:

- hypertension
- angina
- palpitations
- dyspnea
- thrombocytopenia
- sinus tachycardia
- premature ventricular contractions (PVCs)
- chest pain (unspecified)
- hypotension
- hypokalemia
- myoclonia
- phlebitis
- eosinophilia

Mild:

- headache
- nausea
- injection site reaction
- fever

- rash (unspecified)

Administration:

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.
Premixed bags of dobutamine in 5% Dextrose Injection solutions may exhibit a pink color that, if present, will increase with time. This color change is due to slight oxidation of the drug, but there is no significant loss of potency.

Intravenous Administration

Dilution
Concentrate for injection must be diluted with a compatible IV solution (e.g., 5% Dextrose Injection, 10% Dextrose Injection, 0.9% Sodium Chloride Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, Lactated Ringer's Injection) prior to administration.
Institute for Safe Medication Practices (ISMP)/Vermont Oxford Network (VON) Recommended Standard Concentration for Neonatal Infusions: 2,000 mcg/mL
Maximum concentration should not exceed 5,000 mcg/mL.

Intravenous Infusion Administration
Administer diluted solution by IV infusion using a controlled infusion device.
Infuse into a large vein whenever possible.
Use caution to avoid inadvertent bolus administration or inadvertent interruption of the infusion, particularly during line changes, when flushing the line, or during syringe/bag changes.
Do not administer dobutamine simultaneously with solutions containing sodium bicarbonate or strong alkaline solutions (incompatible). Solutions containing dextrose should not be administered through the same administration set as blood, as this may cause pseudoagglutination or hemolysis.
Initiate infusion at a low rate and titrate every few minutes to reach the optimal dosage based on patient response. Dosage titration is guided by the patient's response, including systemic blood pressure, urine flow, frequency of ectopic activity, heart rate, and (whenever possible) measurements of cardiac output, central venous pressure, and/or pulmonary capillary wedge pressure.

Other Injectable Administration

Intraosseous infusion
NOTE: Dobutamine is not approved by the FDA for intraosseous administration.
During cardiopulmonary resuscitation, the same dosage may be given via the intraosseous route when IV access is not available.

Intravenous dosage

Adults

Initially 0.5 to 1 mcg/kg/minute as a continuous IV infusion, then titrated every few minutes. The usual dosage range is 2 to 20 mcg/kg/minute IV. Another manufacturer recommends a usual dosage range of 2.5 to 15 mcg/kg/minute IV. Titrate dosage based on hemodynamic response, including systemic blood pressure, urine flow, frequency of ectopic activity, heart rate, and (whenever possible) measurements of cardiac output, central venous pressure, and/or pulmonary capillary wedge pressure. Infusion rates higher than 20 mcg/kg/minute may produce tachycardia or ventricular

ectopy. On rare occasions, infusion rates up to 40 mcg/kg/minute IV have been required to obtain the desired clinical response. Septic shock clinical practice guidelines recommend dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressors. Titrate to an endpoint reflecting perfusion; reduce rate or discontinue if worsening hypotension or arrhythmias occur.

Infants, Children, and Adolescents

0.5 to 1 mcg/kg/minute as a continuous IV infusion, then titrated every few minutes to clinical response. The usual dosage range is 2 to 20 mcg/kg/minute IV. Infusion rates higher than 20 mcg/kg/minute may produce tachycardia or ventricular ectopy. On rare occasions, infusion rates up to 40 mcg/kg/minute IV have been required to obtain the desired clinical response. If IV access is not available during hypotensive states post-cardiopulmonary resuscitation, the same dobutamine dosage listed for IV use may be administered using the intraosseous route (IO).

Neonates

0.5 to 1 mcg/kg/minute as a continuous IV infusion initially, then titrated every few minutes to clinical response. The usual dosage range is 2 to 20 mcg/kg/minute IV. Infusion rates higher than 20 mcg/kg/minute may produce tachycardia or ventricular ectopy. Because of variation in development, there is significant interpatient variability in response to dobutamine in neonates. Very preterm neonates are likely to have an attenuated reduction in systemic vascular resistance (SVR) compared to term neonates and, therefore, experience a more pronounced increase in blood pressure.

†Indicates off-label use

Supply: Dobutamine Hydrochloride, Dextrose/Dobutamine, Dextrose Intravenous Sol: 250-5%
Dobutamine/Dobutamine Hydrochloride/Dobutamine Hydrochloride, Dextrose/Dobutamine, Dextrose/Dobutrex Intravenous Inj Sol: 1mL, 12.5mg, 20mL, 250mg, 1000-5%, 250-5%, 500-5%

Notes:

- Continuous hemodynamic monitoring and cardiac monitoring is essential.
- Administer via central venous access whenever possible; peripheral administration may cause tissue necrosis with extravasation.
- Use with **nitroprusside**; may have a synergistic effect on ↑ cardiac output.
- **Beta blockers** may negate the effect of dobutamine.
- ↑ risk of arrhythmias or hypertension with some **anesthetics** (**cyclopropane** , **halothane**), **MAO inhibitors** , **oxytocics** , or **tricyclic antidepressants** .

Enalapril, Enalaprit (Vasotec®)

Scope | | **CCT**

Generic Name: **Enalapril, Enalaprit**

Trade Name: **Vasotec®**

Chemical Class: ACE Inhibitor

Therapeutic Class: Antihypertensives

Actions: Angiotensin-converting enzyme (ACE) inhibitors block the conversion of angiotensin I to the vasoconstrictor angiotensin II. ACE inhibitors also prevent the degradation of bradykinin and other vasodilatory prostaglandins. ACE inhibitors also ↑ plasma renin levels and ↓ aldosterone levels. Net result is systemic vasodilation.

Therapeutic Effect(s):

- Lowering of BP in patients with hypertension.
- Increased survival and reduction of symptoms in patients with symptomatic heart failure.
- Decreased development of overt heart failure.

Pharmacokinetics: **Absorption:** *Enalapril:* 55–75% absorbed following oral administration. IV administration results in complete bioavailability.

Distribution: Crosses the placenta; small amounts enter breast milk.

Metabolism and Excretion: Converted by the liver to enalaprilat, the active metabolite; primarily eliminated by kidneys.

Half-life: *Enalapril:* Adults: 2 hr; Adults with HF: 3.4–5.8 hr; Children and infants with HF: 2.7 hr; Neonates with HF: 10.3 hr; *Enalaprilat:* Adults: 35–38 hr; Children and infants with HF: 11.1 hr; Infants 6 wks–8 mo: 6–10 hr; Neonates with HF: 11.9 hr.

TIME/ACTION PROFILE (effect on BP–single dose†)

ROUTE	ONSET	PEAK	DURATION
Enalapril PO	1 hr	4–8 hr	12–24 hr
Enalaprilat IV	15 min	1–4 hr	4–6 hr

†Full effects may not be noted for several weeks.

Indications:

- Alone or with other agents in the management of hypertension.
- Management of symptomatic heart failure.
- Slowed progression of asymptomatic left ventricular dysfunction to overt heart failure.

Unlabeled Use(s):

Treatment of proteinuria in steroid-resistant nephrotic syndrome patients.

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity
- History of angioedema (either idiopathic or with previous use of ACE inhibitors)
- Concurrent use with aliskiren in patients with diabetes or moderate-to-severe renal impairment (CCr <60 mL/min)
- OB: Can cause injury or death of fetus – if pregnancy occurs, discontinue immediately.
- Lactation: Discontinue drug or use formula.

Use Cautiously in:

- Patients with renal impairment, hypovolemia, hyponatremia, and concurrent diuretic therapy

- Black patients (monotherapy of hypertension less effective, may require additional therapy; higher risk of angioedema)
- Surgery/anesthesia (hypotension may be exaggerated)
- Women of childbearing potential
- Pedi: Injectable product contains benzyl alcohol which is associated with gasping syndrome in neonates
- Geri: Initial dose ↓ recommended.

Exercise Extreme Caution in:

Family history of angioedema.

Precautions:

- **Hepatic Impairment**
  Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
- **Renal Impairment**
  CrCl more than 30 mL/minute/1.73 m2: No adjustment necessary.

  CrCl 30 mL/minute/1.73 m2 or less: In adult patients, reduce initial dose to 2.5 mg PO once daily. The dose may be titrated upward gradually. The initial intravenous dose should be 0.625 mg IV. After 1 hour, if there is an inadequate response, an additional dose of 0.625 mg IV may be given. Thereafter, doses of 1.25 mg IV may be administered at 6 hour intervals. Use is not recommended in pediatric patients as data are unavailable.

  Intermittent hemodialysis
  2.5 mg PO after hemodialysis on dialysis days; dosage on non-dialysis days should be adjusted based on clinical response. The starting IV dose for patients receiving dialysis is 0.625 mg (administered IV over at least 5 minutes and preferably up to 1 hour) every 6 hours. Specific recommendations for pediatric patients receiving hemodialysis are not available.

Pregnancy Cat: **Enalapril, Enalaprit** is classified as FDA pregnancy risk category D

Side Effects:

CNS: dizziness, fatigue, headache, vertigo, weakness
Resp: *cough*
CV: *hypotension*, chest pain
GI: abdominal pain, diarrhea, nausea, vomiting
GU: *proteinuria*, impaired renal function
Derm: rashes
F and E: hyperkalemia
Resp: dyspnea
Misc: ANGIOEDEMA
* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Hypertension
IV: (Adults) 0.625–1.25 mg (0.625 mg if receiving diuretics) every 6 hr; can be titrated up to 5 mg every 6 hr.

IV: (Children >1 mo): 5–10 mcg/kg/dose given q 8–24 hr.

Renal Impairment

PO: IV: (Adults) *CCr 10–50 mL/min*– 75% of dose; *CCr <10 mL/min*– 50% of dose.

Renal Impairment

PO: IV: (Children >1 mo): *CCr <30 mL/min*– Contraindicated.

Heart Failure

PO: (Adults) 2.5 mg 1–2 times daily, titrated up to target dose of 10 mg twice daily; initiate therapy at 2.5 mg once daily in patients with hyponatremia (serum sodium <130 mEq/L).

Asymptomatic Left Ventricular Dysfunction

PO: (Adults) 2.5 mg twice daily, titrated upward to a target dose of 10 mg twice daily.

Supply: **Enalaprilat**

Injection: 1.25 mg/mL

Notes: BOXED WARNING

Neonates, pregnancy

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, enalapril should be discontinued as soon as possible. Women of child-bearing age should be made aware of the potential risk and ACE inhibitors should only be given after careful counseling and consideration of individual risks and benefits. Rarely (probably less often than once per 1,000 pregnancies), no alternative to ACE inhibitors will be found. In these rare cases, the pregnant women should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment. The reported adverse fetal and neonatal effects (e.g., hypotension, neonatal skull hypoplasia and craniofacial deformation, fetal limb contractures, hypoplastic lung development, anuria, oligohydramnios, reversible or irreversible renal failure, and death) have been reported during ACE inhibitor exposure during the second and third trimesters. An observational study based on Tennessee Medicaid data reported that the risk of congenital malformations is significantly increased during first-trimester exposure to ACE inhibitors as well. However, a much larger observational study (n = 465,754) found that the risk of birth defects was similar in babies exposed to ACE inhibitors during the first trimester, in those exposed to other antihypertensives during the first trimester, and in those whose mothers were hypertensive but were not treated. Newborns born to mothers with hypertension, either treated or untreated, had a higher risk of birth defects than those born to mothers without hypertension. The authors concluded that the presence of hypertension likely contributed to the development of birth defects rather than the use of medications. Further evaluation of teratogenicity data associated with ACE inhibitor exposure during pregnancy is ongoing. Closely observe neonates with histories of in utero exposure to enalapril for hypotension, oliguria, and hyperkalemia. If oliguria or hypotension occurs, blood pressure and renal perfusion support may be required, as well as exchange transfusion or dialysis to reverse hypotension and/or support decreased renal function. Enalapril, which crosses the placenta, has been removed from neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure.

- Correct volume depletion, if possible, before initiation of therapy due to possible precipitous drop in BP during first 1–3 hr following first dose. Risk of

hypotension may be decreased by discontinuing diuretics or cautiously increasing salt intake 2–3 days prior to beginning enalapril. Monitor BP closely. Resume diuretics if BP is not controlled.

- **PO:** For patients with difficulty swallowing tablets, pharmacist may prepare oral solution. Shake solution before each use. Solution is stable at controlled room temperature for 60 days.
- **IV Administration**
- **IV Push: Diluent:** May be administered undiluted.
- **Rate:** Administer over at least 5 min.
- **Intermittent Infusion: Diluent:** Dilute in D5W, 0.9% NaCl, D5/0.9% NaCl, or D5/LR. Diluted solution is stable for 24 hr at room temperature. **Concentration:** 25 mcg/mL.
- **Rate:** Administer as a slow infusion over at least 5 min.

Esmolol (Brevibloc®)

Scope CCT

Generic Name:	**Esmolol**
Trade Name:	Brevibloc®
Chemical Class:	Selective Beta-Blocker
Therapeutic Class:	cardioselective beta1 receptor blocker with rapid onset, a very short duration of action, and no significant intrinsic sympathomimetic or membrane stabilizing activity at therapeutic dosages.
Actions:	Extremely short-acting, beta1-selective beta-blocker used IV for acute control of HTN or certain supraventricular arrhythmias in the periop, postop, or emergency setting; other uses include acute control of perioperative HTN, management of tachyarrhythmias complicating AMI, and minimization of ischemia secondary to AMI or unstable angina.
Pharmacokinetics:	Onset. “Extremely rapid” Peak. 5 min. Duration 20 min. $t_{½}$ =9 min.
Indications:	• For short-term control of supraventricular tachyarrhythmias, including sinus tachycardia or paroxysmal supraventricular tachycardia (PSVT), or to control ventricular rate in patients with atrial fibrillation or atrial flutter. (It is also used for Hypertensive Emergency and in MI.
Contraindications/ Precautions:	**Acute bronchospasm, asthma, bronchitis, chronic obstructive pulmonary disease (COPD), emphysema, pulmonary disease** Esmolol should not be used in patients with a pulmonary disease such as bronchial asthma, acute bronchospasm, or chronic obstructive pulmonary disease (COPD) (e.g., emphysema or bronchitis) because of potential beta-adrenergic inhibition of bronchodilation (with high doses). **Acute heart failure, AV block, bradycardia, cardiogenic shock, hypotension, pheochromocytoma, pulmonary edema, sick sinus syndrome, vasospastic angina, ventricular dysfunction** Because esmolol depresses conduction through the AV node, it is contraindicated in patients with severe bradycardia or advanced AV block (second or third-degree AV

block) unless a functioning pacemaker is present. Similarly, esmolol should not be used in patients with sick sinus syndrome unless a functioning pacemaker is in place. Esmolol is also contraindicated in patients with cardiogenic shock, acute pulmonary edema, or decompensated acute heart failure, particularly in those with severely compromised left ventricular dysfunction, because the negative inotropic effect of these drugs can further depress cardiac output. In stable patients with heart failure, however, low-doses of beta-blockers (e.g., bisoprolol, carvedilol, metoprolol) have been documented to be beneficial. Many beta-blockers are used in the treatment of hypertrophic cardiomyopathy. Beta-blocker monotherapy should be used with caution in patients with a pheochromocytoma or vasospastic angina (Prinzmetal's angina) because of the risk of hypertension secondary to unopposed alpha-receptor stimulation. In patients with pheochromocytoma, an alpha-blocking agent should be used prior to the initiation of any beta-blocker. Esmolol should only be used with extreme caution in patients with hypotension.

Abrupt discontinuation

Unlike other beta-blockers, abrupt discontinuation of esmolol infusions has not been reported to result in withdrawal effects. However, caution is suggested by the manufacturer when abruptly discontinuing esmolol IV infusions in patients with coronary artery disease. In general, abrupt discontinuation of any beta-adrenergic blocking agent can result in the development of myocardial ischemia, myocardial infarction, ventricular arrhythmias, or severe hypertension, particularly in patients with preexisting cardiac disease. Heart rate increases moderately above pretreatment measurements approximately 30 minutes after discontinuation of esmolol therapy.

Cerebrovascular disease

Because of potential effects of beta-blocks on blood pressure and pulse, esmolol should be used with caution in patients with cerebrovascular insufficiency (cerebrovascular disease) or stroke. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of beta-blocker, alternative therapy should be considered.

Peripheral vascular disease, Raynaud's phenomenon

Administration of esmolol can exacerbate Raynaud's phenomenon or peripheral vascular disease because beta-blockade can indirectly cause peripheral arterial insufficiency due to unopposed alpha-stimulation.

Diabetes mellitus

Esmolol should be used with caution in patients with poorly controlled diabetes mellitus, particularly brittle diabetes. Beta-blockers can prolong or enhance hypoglycemia by interfering with glycogenolysis; this effect may be less pronounced with beta-1 selective beta-blockers than with nonselective agents. Beta-blockers can also mask signs of hypoglycemia, especially tachycardia, palpitations, and tremors; in contrast, diaphoresis and the hypertensive response to hypoglycemia are not suppressed with beta-blockade. Beta-blockers can occasionally cause hyperglycemia. This is thought to be due to blockade of beta-2 receptors on pancreatic islet cells, which would inhibit insulin secretion. Thus, blood glucose

levels should be monitored closely if a beta-blocker is used in a patient with diabetes mellitus.

Hyperthyroidism, thyroid disease, thyrotoxicosis

Beta-blockers should be used with caution in patients with hyperthyroidism or thyrotoxicosis because ß-blockade can mask tachycardia, which is a useful monitoring parameter in thyroid disease. Abrupt withdrawal of beta-blockers in a patient with hyperthyroidism can precipitate thyroid storm. Note that beta-blockers (particularly atenolol, propranolol and esmolol) are, in general, very useful for the acute symptomatic treatment of the thyrotoxic patient by reducing tachycardia or preventing tachyarrhythmias, tremor, anxiety, palpitations, etc. until the patient is euthyroid.

Myasthenia gravis

Esmolol can produce a myasthenic condition that manifests as ptosis, weakness of limbs, and double vision; therefore, esmolol should be avoided in patients with myasthenia gravis.

Renal disease, renal failure, renal impairment

Esmolol should be used with caution in patients with renal disease (e.g., renal failure, renal impairment) because accumulation of the de-esterified metabolite that normally has minimal pharmacologic activity can become clinically significant. Although unlikely, dosage adjustment may be necessary in cases of severe renal impairment.

Extravasation

Avoid extravasation of esmolol during intravenous administration. Sloughing of the skin and necrosis have been reported following infiltration and extravasation of IV esmolol infusions.

Geriatric

Geriatric patients may have unpredictable responses to beta-blockers (increased or decreased sensitivity). Esmolol can be titrated to achieve clinical goals in elderly patients. The federal Omnibus Budget Reconciliation Act (OBRA) regulates medication use in residents of long-term care facilities; esmolol is not commonly given in skilled care residents due to the need for continuous intravenous infusion. According to the OBRA guidelines, antihypertensive regimens should be individualized to achieve the desired outcome while minimizing adverse effects. Antihypertensives may cause dizziness, postural hypotension, fatigue, and there is an increased risk for falls. Additionally, beta-blockers are associated with depression, bronchospasm, cardiac decompensation that may require dose adjustments in those with acute heart failure, and they may mask some symptoms of hypoglycemia (e.g., tachycardia). Beta-blockers metabolized in the liver may have an increased effect or accumulate in those with hepatic impairment. There are many drug interactions that can potentiate the effects of antihypertensives. Beta-blockers may cause or exacerbate bradycardia, particularly in patients receiving other medications that affect cardiac conduction. When discontinuing, a gradual taper may be required to avoid adverse consequences caused by abrupt discontinuation. The OBRA guidelines also caution that antiarrhythmic agents can have serious adverse effects

(e.g., impairment of mental function, appetite, behavior, heart function, or falls) in older individuals.

Breast-feeding

According to the manufacturer, it is not known if esmolol is excreted into human milk and therefore the drug should be used with caution in breast-feeding women. Based on pharmacokinetic parameters (i.e., very short half-life and poor oral bioavailability), short-term exposure esmolol would not be expected to pose a significant risk to a nursing infant. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

Beta-blocker hypersensitivity

Esmolol is contraindicated in patients exhibiting hypersensitivity to the drug or any of its excipients. Do not use esmolol in patients with known beta-blocker hypersensitivity. Cross-sensitivity between beta-blockers may occur

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Precautions:

- **Hepatic Impairment-** No dosage adjustment is needed.
- **Renal Impairment-** No dosage adjustment is needed. The manufacturer advises caution in patients with renal impairment. The minor active metabolite (1/1500 activity of esmolol) is renally excreted and its half-live is increased 10—fold in end-stage renal disease.

Pregnancy Cat.

Esmolol is classified in FDA pregnancy category C. There are no adequate and well-controlled studies in pregnant women; however, use of esmolol in the last trimester of pregnancy or during labor and obstetric delivery has resulted in fetal bradycardia which continued after termination of the infusion. According to the manufacturer, esmolol should be used during pregnancy only if the potential benefit to the mother justifies the risk to the fetus.

Side Effects:

Severe

pulmonary edema / Early / 0-1.0
AV block / Early / 0-1.0
bradycardia / Rapid / 0-1.0
skin necrosis / Early / 0-1.0
tissue necrosis / Early / 0-1.0
bronchospasm / Rapid / 0-1.0
seizures / Delayed / 0-1.0
cardiac arrest / Early / Incidence not known

Moderate

hypotension / Rapid / 20.0-50.0
confusion / Early / 2.0-2.0
chest pain (unspecified) / Early / 0-1.0
constipation / Delayed / 0-1.0
phlebitis / Rapid / 0-1.0

wheezing / Rapid / 0-1.0
dyspnea / Early / 0-1.0
depression / Delayed / 0-1.0
hyperglycemia / Delayed / Incidence not known
hypoglycemia / Early / Incidence not known

Administration:

Adult Initially, a loading dose of 500 mcg/kg IV over 1 minute may be administered. Begin maintenance infusion rate at 50 mcg/kg/minute IV for 4 minutes. If tachycardia is not controlled, the loading dose may be repeated and/or maintenance infusion increased to 100 mcg/kg/minute IV for 4 minutes. May repeat loading dose and increase maintenance infusion by 50 mcg/kg/minute increments every 4 minutes up to 200 mcg/kg/minute. Clinical practice guidelines recommend the use of intravenous beta blockers to slow the ventricular heart rate in the acute setting in patients with atrial fibrillation without pre-excitation; cautious use is needed in patients with heart failure with overt congestion, hypotension, or reduced left ventricular ejection fraction. Although the maximum maintenance infusion recommended in clinical practice guidelines is 300 mcg/kg/minute, dosages as high as 300 mcg/kg/minute provide little added benefit and increase the rate of adverse effects. Dosages higher than 200 mcg/kg/minute are not recommended by the manufacturer. The average effective dose for the treatment of SVT is approximately 100 mcg/kg/minute although dosages as low as 25 mcg/kg/minute have been effective in some patients.
Avoid extravasation; sloughing of the skin and necrosis have been reported following infiltration and extravasation of intravenous esmolol infusions.

Pediatric A total loading dose of 600 mcg/kg IV over 2 minutes was used safely in a study of 20 patients (age 2—16 years). Following the loading dose, the maintenance infusion was started at 200 mcg/kg/minute IV and titrated upward by 50—100 mcg/kg/minute every 5—10 minutes, until a reduction of > 10% in heart rate or blood pressure was observed. The mean maintenance dose to achieve beta-blockade was 550 mcg/kg/minute, and doses as high as 1000 mcg/kg/minute were used.

Supply: Intravenous Inj Sol: 1mL, 10mg, 20mg

Notes:

- **SOME** DRUG INTERACTIONS
- **Acetaminophen; Aspirin, ASA; Caffeine:** (Moderate) Concurrent use of beta-blockers with aspirin and other salicylates may result in loss of antihypertensive activity due to inhibition of renal prostaglandins and thus, salt and water retention and decreased renal blood flow.
- **Adenosine:** (Moderate) Because the pharmacologic effects of beta-blockers include depression of AV nodal conduction and myocardial function, additive effects are possible when used in combination with adenosine. The risk of additive inhibition of AV conduction is symptomatic bradycardia with hypotension or advanced AV block; whereas additive negative inotropic effects could precipitate overt heart failure in some patients.
- **Alpha-blockers:** (Moderate) Orthostatic hypotension may be more likely if beta-blockers are coadministered with alpha-blockers.

- **Amiodarone:** (Major) Amiodarone prolongs AV nodal refractory period and decreases sinus node automaticity. Because beta-blockers have similar effects, concomitant administration of beta-blockers with amiodarone may cause additive electrophysiologic effects (slow sinus rate or worsen AV block), resulting in symptomatic bradycardia, sinus arrest, and atrioventricular block. This is particularly likely in patients with preexisting partial AV block or sinus node dysfunction. While combination amiodarone and beta-blockers should be used cautiously and with close monitoring, it should be noted that post-hoc analysis of amiodarone therapy in patients after acute myocardial infarction in two clinical trials revealed that amiodarone in addition to a beta-blocker significantly lowered the incidence of cardiac and arrhythmic death or resuscitated cardiac arrest when compared with amiodarone or beta-blocker therapy alone.
- **Amlodipine:** (Moderate) Coadministration of amlodipine and beta-blockers can reduce angina and improve exercise tolerance. When these drugs are given together, however, hypotension and impaired cardiac performance can occur, especially in patients with left ventricular dysfunction, cardiac arrhythmias, or aortic stenosis.
- **Beta-agonists:** (Moderate) Use of a beta-1-selective (cardioselective) beta blocker is recommended whenever possible when this combination of drugs must be used together. Monitor the patients lung and cardiovascular status closely. Beta-agonists and beta-blockers are pharmacologic opposites, and will counteract each other to some extent when given concomitantly, especially when non-cardioselective beta blockers are used. Beta-blockers will block the pulmonary effects of inhaled beta-agonists, and in some cases may exacerbate bronchospasm in patients with reactive airways. Beta-agonists can sometimes increase heart rate or have other cardiovascular effects, particularly when used in high doses or if hypokalemia is present.
- **Bupivacaine; Lidocaine:** (Major) Drugs such as beta-blockers that decrease cardiac output reduce hepatic blood flow and thereby decrease lidocaine hepatic clearance. Also, opposing effects on conduction exist between lidocaine and beta-blockers while their effects to decrease automaticity may be additive. Propranolol has been shown to decrease lidocaine clearance and symptoms of lidocaine toxicity have been seen as a result of this interaction. This interaction is possible with other beta-blocking agents since most decrease hepatic blood flow. Monitoring of lidocaine concentrations is recommended during concomitant therapy with beta-blockers. (Moderate) Local anesthetics may cause additive hypotension in combination with antihypertensive agents. Use extreme caution with the concomitant use of bupivacaine and antihypertensive agents. Peripheral vasodilation may occur after use of bupivacaine. Thus, patients receiving antihypertensive agents may experience additive hypotensive effects. Blood concentrations of local anesthetics achieved after therapeutic doses are associated with minimal change in peripheral vascular resistance. Higher blood concentrations of local anesthetics may occur due to inadvertent intravascular administration or repeated doses
- **Clonidine:** (Major) Monitor heart rate in patients receiving concomitant clonidine and agents known to affect sinus node function or AV nodal conduction (e.g., beta-blockers). Severe bradycardia resulting in hospitalization and pacemaker insertion has been reported during combination therapy with clonidine and other sympatholytic agents. Concomitant use of clonidine with beta-blockers can also cause additive hypotension. Beta-blockers should not be substituted for clonidine when modifications are made in a patient's antihypertensive regimen because beta-blocker administration during clonidine withdrawal can augment clonidine withdrawal, which may lead to a hypertensive crisis. If a beta-blocker is to be substituted for clonidine, clonidine should be gradually tapered and the beta-blocker should be gradually increased over several days to avoid the

possibility of rebound hypertension; administration of beta-blockers during withdrawal of clonidine can precipitate severe increases in blood pressure as a result of unopposed alpha stimulation.

- **Digoxin:** (Moderate) A potentially clinically significant interaction between esmolol and digoxin may exist due to their additive effects on the AV node. The efficacy of esmolol in controlling ventricular response and in conversion to sinus rhythm may be improved with preoperative digitalization or with subsequent concomitant therapy for new-onset atrial fibrillation or flutter. The concomitant administration of esmolol and digoxin resulted in a 10-20% increase in serum digoxin concentrations. The clinical significance of this interaction is not known; however, the manufacturer warns that esmolol should be titrated cautiously in patients receiving digoxin.
- **Etomidate:** (Major) General anesthetics can potentiate the antihypertensive effects of beta-blockers and can produce prolonged hypotension. Beta-blockers may be continued during general anesthesia as long as the patient is monitored for cardiac depressant and hypotensive effects.
- **Fentanyl:** (Moderate) The risk of significant hypotension and/or bradycardia during therapy with fentanyl is increased in patients receiving beta-blockers. In addition, increased concentrations of fentanyl may occur if it is coadministered with carvedilol; exercise caution. Carvedilol is a P-glycoprotein (P-gp) inhibitor and fentanyl is a P-gp substrate. If these drugs are coadministered, the fentanyl dose may need to be very conservative, and the patient should be carefully monitored for an extended time period for signs of too much fentanyl such as oversedation, respiratory depression, and hypotension.
- **General anesthetics:** (Major) General anesthetics can potentiate the antihypertensive effects of beta-blockers and can produce prolonged hypotension. Beta-blockers may be continued during general anesthesia as long as the patient is monitored for cardiac depressant and hypotensive effects.
- **Glucagon:** (Minor) Because beta-blockers blunt sympathomimetic-mediated hepatic gluconeogenesis, beta-blockers can inhibit the hyperglycemic actions of glucagon. In addition, intravenous administration of glucagon has been shown to have positive inotropic and chronotropic effects. A transient increase in both blood pressure and pulse rate may occur following the administration of glucagon, especially in patients taking beta-blockers. Clinicians should be aware of these opposing pharmacologic actions of glucagon and beta-blockers.
- **Haloperidol:** (Moderate) Haloperidol should be used cautiously with esmolol due to the possibility of additive hypotension.
- **Insulins:** (Moderate) Although no pharmacokinetic interaction has been observed between beta-blockers and antidiabetic agents, patients receiving beta-blockers and insulin concomitantly should be closely monitored for an inappropriate response. Beta-blockers exert complex actions on the body's ability to regulate blood glucose. Because of this, beta-blockers may cause a pharmacodynamic interaction with antidiabetic agents. Beta-blockers can prolong hypoglycemia by interfering with glycogenolysis (secondary to blocking the compensatory actions of epinephrine) or can promote hyperglycemia (by inhibiting insulin secretion and decreasing tissue sensitivity to insulin). Furthermore, a prospective trial in non-diabetic patients with hypertension indicated that treatment with beta-blockers increased the risk of the development of diabetes by 28% at six years. In addition, beta-blockers may mask the signs and symptoms of hypoglycemia, specifically the tachycardic response, and exaggerate the hypertensive response to hypoglycemia. Selective beta-blockers, such as acebutolol, atenolol, or metoprolol, can cause fewer problems with blood glucose regulation, although these agents can still mask the symptoms of hypoglycemia. While beta-blockers may have negative effects on glycemic

control, they reduce the risk of cardiovascular disease and stroke in patients with diabetes. Furthermore, their use should not be avoided in patients with compelling indications for beta-blocker therapy (i.e., post-MI, heart failure, etc.) when no other contraindications are present. Decreased mortality has been shown in the post-MI and heart failure populations when beta-blockers are used, especially in patients with coexisting diabetes mellitus.

- **Ketamine:** (Major) General anesthetics can potentiate the antihypertensive effects of beta-blockers and can produce prolonged hypotension. Beta-blockers may be continued during general anesthesia as long as the patient is monitored for cardiac depressant and hypotensive effects.
- **Lidocaine:** (Major) Drugs such as beta-blockers that decrease cardiac output reduce hepatic blood flow and thereby decrease lidocaine hepatic clearance. Also, opposing effects on conduction exist between lidocaine and beta-blockers while their effects to decrease automaticity may be additive. Propranolol has been shown to decrease lidocaine clearance and symptoms of lidocaine toxicity have been seen as a result of this interaction. This interaction is possible with other beta-blocking agents since most decrease hepatic blood flow. Monitoring of lidocaine concentrations is recommended during concomitant therapy with beta-blockers.
- **Milrinone:** (Moderate) Concurrent administration of antihypertensive agents could lead to additive hypotension when administered with milrinone. Titrate milrinone dosage according to hemodynamic response.
- **Morphine:** (Moderate) Morphine increases the steady-state blood concentrations of esmolol by 50%, although morphine blood concentrations are not affected by esmolol. Careful titration of esmolol is prudent when given with morphine.
- **Nitroglycerin:** (Moderate) Nitroglycerin can cause hypotension. This action may be additive with vasodilators. Patients should be monitored more closely for hypotension if nitroglycerin, including nitroglycerin rectal ointment, is used concurrently with any beta-blockers.other agents that can cause hypotension such as antihypertensive agents or other peripheral
- **Octreotide:** (Moderate) Dose adjustments in drugs such as beta-blockers and calcium-channel blockers which cause bradycardia and/or affect cardiac conduction may be necessary during octreotide therapy due to additive effects.
- **Procainamide:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like esmolol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension.
- **Propofol:** (Major) General anesthetics can potentiate the antihypertensive effects of beta-blockers and can produce prolonged hypotension. Beta-blockers may be continued during general anesthesia as long as the patient is monitored for cardiac depressant and hypotensive effects.
- **Rocuronium:** (Moderate) Esmolol, given 30 seconds before rocuronium, prolonged the onset of rocuronium by 30 seconds. Heart rate and blood pressure were not affected. The clinical significance of this interaction is unknown; patients should be monitored closely if esmolol and rocuronium are used concomitantly.
- **Succinylcholine:** (Moderate) Beta-blockers can enhance the neuromuscular blocking activity of succinylcholine.

- **Sufentanil:** (Moderate) The incidence and degree of bradycardia and hypotension during induction with sufentanil may be increased in patients receiving beta-blockers.
- **Sympathomimetics:** (Major) Sympathomimetics, such as amphetamines, phentermine, and decongestants (e.g., pseudoephedrine, **phenylephrine**), and many other drugs, may increase both systolic and diastolic blood pressure and may counteract the activity of the beta-blockers. Due to the risk of unopposed alpha-adrenergic activity, sympathomimetics should be used cautiously with beta-blockers. Increased blood pressure, bradycardia, or heart block may occur due to excessive alpha-adrenergic receptor stimulation. Close monitoring of blood pressure or the selection of alternative therapeutic agents to the sympathomimetic agent may be needed.
- **Terazosin:** (Moderate) Orthostatic hypotension may be more likely if beta-blockers are coadministered with alpha-blockers.
- **Thiopental:** (Moderate) General anesthetics can potentiate the antihypertensive effects of beta-blockers and can produce prolonged hypotension. Patients receiving beta-blockers before or during surgery involving thiopental should be monitored closely for signs of heart failure.
- **Verapamil:** (Moderate) Oral calcium-channel blockers and beta-blockers like esmolol are used together for their therapeutic benefits to reduce angina and improve exercise tolerance. However, concomitant administration of beta-adrenergic blocking agents and verapamil can lead to significant AV nodal blockade. This can manifest as heart block, bradycardia, cardiac conduction abnormalities and/or prolonged PR interval. Congestive heart failure or severe hypotension also can occur. The combination of beta-blockers and verapamil should be avoided in patients with poor ventricular function due to increased negative inotropic effects.

Etomidate (Amidate®)

Scope CCT

Generic Name:	**Amidate**
Trade Name:	Etomidate
Chemical Class:	Nonbarbituate hypnotic
Therapeutic Class:	anesthesia induction agent
Actions:	Short-Acting hypnotic that causes anesthesia and CNS depression
Pharmacokinetics:	Onset <1 min. Peak 1 min. Duration 5-10 min. $t_{½}$ =.
Indications:	Premedication sedation for RSI
Contraindications:	Hypersensitivity, Labor/delivery
Precautions:	•
Pregnancy Cat.	C. (Use during labor and obstetric delivery (including caesarean section) is not recommended because sufficient data are not available to support its use in this setting.)
Side Effects:	Apnea, , laryngospasm, bradycardia, arrhythmia exacerbation, anaphylactoid reactions, transient muscle movement, myoclonus and tremors that resemble seizure-like activity

Administration:	*Adult* 0.3mg/kg IV over 30-60 seconds
Supply:	40 mg in 20 ml (2 mg/ml)
Notes:	•

Famotidine (Pepcid®)

Scope CCT

Generic Name:	**Famotidine**
Trade Name:	Pepcid
Chemical Class:	Histamine type 2-receptor antagonist
Therapeutic Class:	Histamine blocker
Actions:	Famotidine competitively inhibits the binding of histamine to H2-receptors on the gastric basolateral membrane of parietal cells, reducing basal and nocturnal gastric acid secretions.
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ =2.5-3.5 hours.
Indications:	• gastric or duodenal ulcer, gastroesophageal reflux disease, and pathological hypersecretory conditions.
Contraindications:	• Hypersensitivity to the drug, class or components.
Precautions:	• CrCl < 50 mL/min: reduce recommended dose by 50% (can cause prolongation of QTc in patients with impaired renal function).
Pregnancy Cat.	B
Side Effects:	seizures toxic epidermal necrolysis Stevens-Johnson syndrome anaphylactoid reactions angioedema atrophic gastritis arrhythmia exacerbation AV block agranulocytosis pancytopenia bronchospasm rhabdomyolysis QTc prolongation in renal impaired patients Leukopenia

	Thrombocytopenia Pancytopenia Hepatitis Pneumonia, interstitial
Administration:	Intermittent intravenous injection: Dilute 20 mg of famotidine injection to a total of 5 or 10 mL with 0.9% Sodium Chloride injection or other compatible solution to give concentrations of 4 or 2 mg/mL, respectively. Inject appropriate dose over >= 2 minutes and at a rate <= 10 mg/minute. Intermittent intravenous (IV) infusion using premixed infusion in Galaxy containers: The premixed infusion container contains famotidine 20 mg per 50 mL 0.9% Sodium Chloride injection. Infuse over 15—30 minutes *Adult* 20 mg IV every 12 hours
Supply:	Famotidine/Pepcid Intravenous Inj Sol: 1mL, 10mg, 20mg, 50mL The premixed infusion container contains famotidine 20 mg per 50 mL 0.9% Sodium Chloride injection
Notes:	• Consider for patients who are intubated and have not received any acid reducing medication (H2's or proton pump inhibitors).

Fosphenytoin (Cerebyx®)

Scope CCT

Generic Name:	**Fosphenytoin**
Trade Name:	**Cerebyx®**
Chemical Class:	
Therapeutic Class:	Anticonvulsant
Actions:	• Limits seizure propagation by altering ion transport. • May also decrease synaptic transmission. • Fosphenytoin is rapidly converted to phenytoin, which is responsible for its pharmacologic effects. **Therapeutic Effect(s):** Diminished seizure activity
Pharmacokinetics:	**Absorption:** Rapidly converted to phenytoin after IV administration and completely absorbed after IM administration. **Distribution:** Distributes into CSF and other body tissues and fluids. Enters breast milk; crosses the placenta, achieving similar maternal/fetal levels. Preferentially distributes into fatty tissue. **Protein Binding:** *Fosphenytoin*– 95–99%; *phenytoin*– 90–95%. **Metabolism and Excretion:** Mostly metabolized by the liver; minimal amounts excreted in the urine. **Half-life:** *Fosphenytoin*– 15 min; *phenytoin*– 22 hr (range 7–42 hr). **TIME/ACTION PROFILE (anticonvulsant effect)**

ROUTE	ONSET	PEAK	DURATION
IM	unknown	30 min	up to 24 hr
IV	15–45 min	15–60 min	up to 24 hr

Indications:	• Short-term (<5 day) parenteral management of generalized, convulsive status epilepticus when use of phenytoin is not feasible. • Treatment and prevention of seizures during neurosurgery when use of phenytoin is not feasible
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity; • Sinus bradycardia, sinoatrial block, 2nd- or 3rd-degree AV heart block or Adams-Stokes syndrome; • Concurrent use of delavirdine. **Use Cautiously in:** • Hepatic or renal disease (↑ risk of adverse reactions; dose reduction recommended for hepatic impairment);

- OB: Safety not established; may result in fetal hydantoin syndrome if used chronically or hemorrhage in the newborn if used at term;
- Lactation: Safety not established.

Exercise Extreme Caution in:

Patients positive for HLA-B*1502 allele (unless exceptional circumstances exist where benefits clearly outweigh the risks).

Precautions:

- **Hepatic Impairment**
  Dosage adjustments may be required based upon serum phenytoin concentrations and clinical response. Fosphenytoin is converted to phenytoin in the systemic circulation; phenytoin is primarily metabolized in the liver. Patients with hepatic disease may have an increased fraction of unbound phenytoin. Fosphenytoin clearance to phenytoin may be increased without a similar increase in phenytoin clearance, potentially increasing the frequency and severity of adverse reactions.
- **Renal Impairment**
  Dosing adjustments may be required based upon serum phenytoin concentrations and clinical response. Patients with renal disease may have an increased fraction of unbound phenytoin. Fosphenytoin clearance to phenytoin may be increased without a similar increase in phenytoin clearance, potentially increasing the frequency and severity of adverse reactions. Of note, during the conversion of fosphenytoin to phenytoin, phosphate and formaldehyde are liberated. The phosphate load provided by fosphenytoin (0.0037 mmol phosphate/mg PE) should be considered when treating patients with severe renal impairment.

  Intermittent hemodialysis
  Phenytoin is not significantly removed during a standard hemodialysis session; therefore, supplemental dosing after hemodialysis is not necessary.

Pregnancy Cat: **Fosphenytoin** is classified as FDA pregnancy risk category D

Side Effects:

CNS: *dizziness*, *drowsiness*, *nystagmus*, agitation, brain edema, headache, stupor, vertigo

EENT: amblyopia, deafness, diplopia, tinnitus

CV: hypotension (with rapid IV administration), tachycardia

GI: dry mouth, nausea, taste perversion, tongue disorder, vomiting

Derm: *pruritus*, purple glove syndrome, rash, STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS

MS: back pain

Neuro: *ataxia*, dysarthria, extrapyramidal syndrome, hypesthesia, incoordination, paresthesia, tremor

Misc: DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS), pelvic pain

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Note: Doses of fosphenytoin are expressed as phenytoin sodium equivalents [PE]

Status Epilepticus

IV: (Adults) 15–20 mg PE/kg.

Nonemergent and Maintenance Dosing

IV: IM: (Adults and Children > 16 yr): *Loading dose*– 10–20 mg PE/kg. *Maintenance dose*– 4–6 mg PE/kg/day.

IV: IM: (Children 10–16 yr): 6–7 mg PE/kg/day.

IV: IM: (Children 7–9 yr): 7–8 mg PE/kg/day.

IV: IM: (Children 4–6 yr): 7.5–9 mg PE/kg/day.

IV: IM: (Children 0.5–3 yr): 8–10 mg PE kg/day.

IV: IM: Infants 5 mg PE kg/day.

IV: IM: Neonates 5–8 mg PE/kg/day.

Supply: **Injection:** 50 mg PE/mL

Notes:

- BOXED WARNING

Adams-Stokes syndrome, AV block, bradycardia, bundle-branch block, cardiac arrhythmias, cardiac disease, hypotension, infusion-related reactions, intravenous administration

Fosphenytoin is contraindicated in patients with conduction abnormalities such as sinus bradycardia, sino-atrial block, second or third degree AV block (atrioventricular block) or bundle-branch block, and Adams-Stokes syndrome because of the effect of parenteral phenytoin on ventricular automaticity. Infusion-related reactions, specifically cardiovascular risks (e.g., hypotension, cardiac arrhythmias), have been associated with rapid intravenous infusion rates. The rate of intravenous administration of fosphenytoin is critically important to avoid or limit adverse cardiovascular events; do not exceed recommended infusion rates (i.e., 150 mg PE/minute). In adults with hypotension or other cardiac disease, lower infusion rates may be considered (i.e., 25 to 50 mg PE/minute), if necessary. Careful cardiac monitoring is needed during and after administering intravenous fosphenytoin. Although the risk of cardiovascular toxicity increases with infusion rates above the recommended infusion rate, these events have also been reported at or below the recommended infusion rate. Reduction in rate of administration or discontinuation of

dosing may be needed if cardiovascular adverse events occur during or following intravenous infusion. Adverse cardiovascular reactions include severe hypotension and cardiac arrhythmias. Cardiac arrhythmias have included bradycardia, heart block, QT interval prolongation, ventricular tachycardia, and ventricular fibrillation which have resulted in asystole, cardiac arrest, and death. Cardiovascular adverse events to fosphenytoin occur more often in patients who are elderly or debilitated, children (especially infants), critically ill, or those with pre-existing hypotension or severe myocardial insufficiency or cardiac disease. However, cardiac events have also been reported in adults and children without underlying cardiac disease or comorbidities and at recommended doses and infusion rates.

- Do not confuse concentration of fosphenytoin with total amount of drug in vial.
- The anticonvulsant effect of fosphenytoin is not immediate. Additional measures (including parenteral benzodiazepines) are usually required in the immediate management of status epilepticus. Loading dose of *fosphenytoin* should be followed with the institution of maintenance anticonvulsant therapy.
- **IV Push: Diluent:** D5W or 0.9% NaCl. **Concentration:** 1.5–25 mg PE/mL. May be refrigerated for up to 48 hr.
- **Rate:** Administer at a rate of <150 mg PE/min in adults and <3 mg/kg/min in children to minimize risk of hypotension.

Heparin Sodium®)

Scope | **CCT**

Generic Name:	**Heparin Sodium**
Trade Name:	Heparin, Prefill Advanced Heparin Lock flush
Chemical Class:	glycosaminoglycan anticoagulant
Therapeutic Class:	Platelet Inhibitor (IIB3A)
Actions:	Heparin exerts its anticoagulant action by accelerating the activity of antithrombin III (ATIII) to inactivate thrombin; however, heparin does not lyse existing clots.
Pharmacokinetics:	Onset “almost immediate”. Peak . Duration . $t_{½}$ = The anticoagulation half-life of heparin is 1, 2.5, and 5 hours when heparin 100, 400, or 800 units/kg, respectively, is given intravenously. Heparin is given parenterally, either intravenously or subcutaneously. Because heparin is highly negatively charged, it binds to a variety of plasma proteins (e.g., histidine-rich glycoprotein, vitronectin, lipoproteins, fibronectin, fibrinogen, platelet factor 4, and von Willebrand factor) some of which are acute-phase reactant proteins that are elevated in acute illness or are released from platelet and endothelial cells as part of the clotting process.

Indications:	• **coronary artery thrombosis, PE, DVT**
Contraindications:	• Heparin is contraindicated in patients with severe thrombocytopenia and in those with a history of heparin-induced thrombocytopenia (HIT) or heparin-induced thrombocytopenia and thrombosis (HITT). • Heparin is contraindicated in patients with uncontrollable bleeding (with the exception of bleeding associated with disseminated intravascular coagulation).
Precautions:	Hepatic Impairment It appears that hepatic impairment does not affect the elimination of heparin; however, patients with hepatic disease may have increased risk of bleeding during heparin therapy.
Pregnancy Cat.	In published reports, heparin exposure during pregnancy did not result in increased risk of adverse maternal or fetal outcomes in humans. No teratogenicity was seen in animal studies where animals were given approximately 10 times the maximum recommended human dose during organogenesis; however, increased resorptions were reported. Consider the benefits and risks of heparin to a pregnant woman and possible risks to the fetus when using heparin during pregnancy. Heparin does not cross the placental barrier. When indicated, only preservative-free formulations should be administered. Benzyl alcohol has been associated with serious adverse events and death, particularly in neonates and infants.
Side Effects:	Severe bone fractures, ocular hemorrhage, intracranial bleeding, hematemesis retroperitoneal bleeding, GI bleeding, stroke, yocardial infarction, thrombosis thromboembolism, bronchospasm, anaphylactic shock, anaphylactoid reactions hyperkalemia, skin necrosis
Administration:	*Adult* 60 units/kg IV bolus followed by heparin 12 Units/kg/hour IV *Pediatric* Ask Dr Mel Wright dosage for pediatrics prior to publishing
Supply:	
Notes:	• **Alteplase, tPA:** (Major) An additive risk of bleeding may be seen in patients receiving thrombolytic agents and anticoagulants. • **Protamine:** (Severe) Upon contact with heparin, protamine forms a salt, neutralizing the anticoagulant effect of both drugs. Protamine, a strongly basic compound, forms complexes with heparin sodium or heparin calcium, which are acidic compounds. Formation of this complex can result in disruption of the heparin-antithrombin III complex responsible for the anticoagulant activity of heparin. Protamine is used therapeutically to reverse the activity of heparins.

Hydralazine (Apresoline®)

Scope		**CCT**

Generic Name:	**Hydralazine**
Trade Name:	Apresoline®
Chemical Class:	Vasodilator
Therapeutic Class:	Antihypertensive
Actions:	Hydralazine is a peripheral vasodilator; it causes relaxation of arteriolar smooth muscle via a direct effect. Although stimulation of the sympathetic nervous system is associated with hydralazine administration, this is a compensatory response and not a component of its mechanism. The molecular explanation of hydralazine's mechanism is not fully understood; however, similar to organic nitrates and nitroprusside, it is thought that hydralazine interferes with the calcium movements within vascular smooth muscle that are responsible for initiating and maintaining the contractile state. In contrast to organic nitrates and sodium nitroprusside, however, hydralazine is selective for arterioles. The peripheral vasodilating effects of hydralazine result in decreased arterial blood pressure (diastolic more than systolic) and peripheral vascular resistance. In addition, the hydralazine-induced reflex autonomic response increases heart rate, stroke volume, cardiac output, and left ventricular ejection fraction. The preferential dilation of arterioles, as compared to veins, minimizes postural hypotension and promotes the increase in cardiac output even though the hypotensive effects of hydralazine are diminished somewhat by this increase in cardiac output. There is also evidence suggesting hydralazine exerts a positive inotropic effect on the failing human ventricle. Animal and limited human data indicate that nitric oxide (NO) may be generated from hydralazine that also has an antioxidant quality to enhance the effects of nitrates and to mitigate the tolerance associated with chronic nitrate therapy. The antioxidant effect of hydralazine can be attributed to its ability in inhibiting oxidase formation. The accumulation of oxidative free radicals creates an environment where chronic reductions in NO bioavailability contribute to a loss of skeletal muscle microvessels. This effect, in turn, leads to impaired muscle perfusion with elevated metabolic demand. Studies show that treatment with hydralazine markedly inhibits oxidase which plays a role in regulating the bioactivity of NO, produced either endogenously or when administered exogenously. Cerebral, coronary, splanchnic, and renal blood flow usually increase following administration of hydralazine, while urinary parameters are generally unaffected. Hydralazine increases renin activity in plasma, presumably by the renal juxtaglomerular cells in response to sympathetic nervous system stimulation; the increase in renin activity leads to the production of angiotensin II, which stimulates aldosterone and thus, sodium reabsorption. Due to fluid retention, plasma volume increases. As a result, tolerance can develop, which may account for the absence of improvement in some patients receiving the drug for prolonged periods of time. As an antihypertensive, hydralazine does not lead to improvements in LVH. Hydralazine may actually worsen LVH, potentially due to reflex tachycardia and sympathetic stimulation, which may counteract the benefits of afterload reduction.
Pharmacokinetics:	**Absorption:** Rapidly absorbed following oral administration; well absorbed from IM sites. **Distribution:** Widely distributed. Crosses the placenta; enters breast milk in minimal concentrations. **Metabolism and Excretion:** Mostly metabolized by the GI mucosa and liver by N-acetyltransferase (rate of acetylation is genetically determined [slow acetylators have ↑ hydralazine levels and ↑ risk of toxicity; fast acetylators have ↓ hydralazine levels and ↓ response]).

Half-life: 2–8 hr**.**

TIME/ACTION PROFILE (antihypertensive effect)

ROUTE	ONSET	PEAK	DURATION
PO	45 min	2 hr	2–4 hr
IM	10–30 min	1 hr	3–8 hr
IV	5–20 min	15–30 min	2–6 hr

Indications: Moderate to severe hypertension

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity;
- Some products contain tartrazine and should be avoided in patients with known intolerance**.**

Use Cautiously in:

- Cardiovascular or cerebrovascular disease;
- Severe renal and hepatic disease (dose modification may be necessary);
- OB: Lactation: Has been used safely during pregnancy.

Precautions:

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available. Hydralazine is extensively metabolized in the liver and is subject to polymorphic acetylation; patients with slow acetylation status have higher plasma levels of hydralazine and these patients require lower doses to maintain control of blood pressure.

Renal Impairment

CrCl > 50 mL/min: no dosage adjustment needed.
CrCl 10—50 mL/min: administer every 8 hours.
CrCl < 10 mL/min: administer every 8—16 hours. Interval may be extended to 12—24 hours based on patient response.

Intermittent Hemodialysis:
Administer every 12 to 24 hours depending on patient blood pressure.

Peritoneal Dialysis:
Administer every 12 to 24 hours depending on patient blood pressure.

Pregnancy Cat: Hydralazine is classified as FDA pregnancy risk category C

Side Effects:

Severe:

- myocardial infarction
- ileus

- pericarditis
- glomerulonephritis
- vasculitis
- lupus-like symptoms
- agranulocytosis

Moderate:

- angina
- sinus tachycardia
- palpitations
- edema
- hypotension
- peripheral edema
- peripheral vasodilation
- orthostatic hypotension
- fluid retention
- constipation
- erythema
- hepatitis
- eosinophilia
- peripheral neuropathy
- leukopenia
- anemia
- dyspnea
- splenomegaly
- conjunctivitis
- lymphadenopathy
- depression
- confusion

Administration:

Injectable Administration

Hydralazine can be administered intramuscularly or as a rapid IV injection.
Do not add hydralazine to any IV solutions.
Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.
Administer dose immediately after opening the vial.
Hydralazine changes color after contact with metal, discard any discolored hydralazine solution.
Blood pressure should be checked frequently following administration of injectable hydralazine.

Intravenous Administration

Inject undiluted injection IV via Y-site or a 3-way stopcock at a rate of 10 mg over at least 1 minute.

Intramuscular Administration

No dilution necessary.
Inject deeply into a large muscle. Aspirate prior to injection to avoid injection into a blood vessel.

For the treatment of hypertension.

Intravenous Route

Adults

10—20 mg IV bolus. Repeat as needed, usually every 4—6 hours. Switch to oral antihypertensive therapy as soon as possible, usually within 24—48 hours. When switching from IV to oral therapy, the IV dose should generally be doubled and administered orally; titrate the oral dose to response.

Infants†, Children†, and Adolescents†

Initially, 0.2—0.6 mg/kg/dose IV (up to 20 mg) every 4 hours as needed for blood pressure control. Max: 1.7—3.5 mg/kg/day IV, given in divided doses every 4 hours as needed. Use IV route only if PO is not feasible. Switch to oral therapy as soon as possible, usually with 24—48 hours. When switching from IV to oral therapy, the IV dose should generally be doubled and administered orally; titrate the oral dose to response.

Neonates†

Limited data in neonates. A dose of 0.15—0.6 mg/kg/dose IV administered every 4 hours has been suggested. Repeat as needed for blood pressure control. Only use IV route if PO is not feasible. Switch to oral antihypertensive therapy as soon as possible, usually within 24—48 hours.

For the treatment of hypertension associated with severe preeclampsia or eclampsia.

Intravenous dosage

Adult and Adolescent females

5—10 mg IV over 2 minutes for SBP >= 160 or DBP >= 110 mmHg. Check BP in 20 minutes and if either BP threshold is exceeded, give 10 mg IV over 2 minutes. Check BP in 20 minutes and if either threshold is exceeded, switch to labetalol 20 mg IV over 2 minutes and check BP in 10 minutes. If either BP threshold is still exceeded, give labetalol 40 mg IV over 2 minutes, obtain emergency consultation, and give additional antihypertensive medication per specific order. Once SBP < 160 and DBP < 110, check BP every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then once every hour for 4 hours.

For the treatment of hypertensive emergency or hypertensive urgency.

Intravenous dosage

Adults

Initially, 10—20 mg IV bolus. Repeat as needed, usually every 4—6 hours. Switch to oral antihypertensive therapy as soon as possible, usually within 24—48 hours. When switching from IV to oral therapy, the IV dose should generally be doubled and administered orally; titrate the oral dose to response.

Infants†, Children†, and Adolescents†

Initially, 0.1—0.6 mg/kg/dose IV (up to 20 mg) every 4 hours as needed for blood pressure control. Usual dosage is 1.7—3.5 mg/kg/day IV, given every 4 hours as needed. Switch to oral therapy as soon as possible, usually within 24—48 hours. When switching from IV to oral therapy, the IV

dose should generally be doubled and administered orally; titrate the oral dose to response.

Neonates†

0.15—0.6 mg/kg/dose IV administered every 4 hours. Repeat as needed for blood pressure control. Switch to oral antihypertensive therapy as soon as possible, usually within 24—48 hours. When switching from IV to oral therapy, the IV dose should generally be doubled and administered orally; titrate the oral dose to response.

Intramuscular dosage

Adults

Initially, 10—50 mg IM. Repeat as needed, usually every 4—6 hours initially. Switch to oral antihypertensive therapy as soon as possible, usually within 24—48 hours.

Infants†, Children†, and Adolescents†

Initially, 0.1—0.6 mg/kg/dose IM (up to 20 mg) every 4 hours as needed for blood pressure control. Usual dosage is 1.7—3.5 mg/kg/day IM given every 4 hours as needed. Switch to oral therapy as soon as possible, usually within 24—48 hours.

†Indicates off-label use

Supply: Apresoline/Hydralazine Hydrochloride Oral Tab: 10mg, 25mg, 50mg, 100mg
Hydralazine Hydrochloride Intramuscular Inj Sol: 1mL, 20mg
Hydralazine Hydrochloride Intravenous Inj Sol: 1mL, 20mg

Notes:

- ↑ hypotension with acute ingestion of **alcohol** , other **antihypertensives** , or **nitrates** .
- **MAO inhibitors** may exaggerate hypotension.
- May ↓ pressor response to **epinephrine** .
- **NSAIDs** may ↓ antihypertensive response.
- **Beta blockers** ↓ tachycardia from hydralazine (therapy may be combined for this reason).
- **Metoprolol** and **propranolol** ↑ hydralazine levels.
- ↑ blood levels of **metoprolol** and **propranolol** .

Insulin Regular **(**Humulin R, Novolin R ®**)**

Scope CCT

Generic Name:	**Insulin, regular**
Trade Name:	Humulin R, Novolin R
Chemical Class:	pancreatics
Therapeutic Class:	antidiabetics hormones
Actions:	Lowers blood glucose by: stimulating glucose uptake in the skeletal muscle and fat, inhibiting hepatic glucose production.

Other actions: Inhibition of lipolysis and proteolysis, enhanced protein synthesis.

Pharmacokinetics:

Absorption: Rapidly absorbed from subcutaneous administration sites. U-100 regular insulin is absorbed slightly more quickly than U-500.

Distribution: Identical to endogenous insulin.

Metabolism and Excretion: Metabolized by liver, spleen, kidney, and muscle.

Half-Life: 30-60 min

TIME/ACTION PROFILE (hypoglycemic effect)

ROUTE	ONSET	PEAK	DURATION
Regular insulin IV	10–30 min	15–30 min	30–60 min
Regular insulin subcutaneous	30–60 min	2–4 hr	5–7 hr

Indications:

Control of hyperglycemia in patients with diabetes mellitus.

Unlabeled: Treatment of hyperkalemia

Contraindications/ Considerations:

Contraindicated in:

- Hypoglycemia;
- Allergy or hypersensitivity to a particular type of insulin, preservatives, or other additives.

Use Cautiously in:

- Stress or infection–may temporarily ↑ insulin requirements;
- Renal/hepatic impairment–may ↓ insulin requirements;
- Concomitant use with pioglitazone or rosiglitazone (↑ risk of fluid retention and worsening HF)
- OB: Pregnancy may temporarily ↑ insulin requirements

Precautions:

- **Hepatic Impairment:** Frequent blood glucose monitoring and insulin dosage reduction may be required in patients with hepatic impairment. Individualize dosage based on blood glucose and other clinical parameters.

- **Renal Impairment:** Frequent blood glucose monitoring and insulin dosage reduction may be required in patients with renal impairment.

Individualize dosage based on blood glucose and other clinical parameters.

Pregnancy Cat:

Insulin, regular is classified as FDA pregnancy risk category B

Side Effects:

Endo: HYPOGLYCEMIA

F and E: hypokalemia

Local: lipodystrophy, pruritus, erythema, swelling

Misc: ALLERGIC REACTIONS INCLUDING ANAPHYLAXIS

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

IV:	0.1 units/kg/hr as a continuous infusion
Subcutaneous:	0.5 – 1 units/kg/day in divided doses. (Need Sliding Scale)

*Give **no more** than 30 minutes prior to food or snack.*

Supply: 100 units/ml

Notes:

- **High Alert:** Medication errors involving insulins have resulted in serious patient harm and death. Clarify all ambiguous orders and do not accept orders using the abbreviation "u" for units, which can be misread as a zero or the numeral 4 and has resulted in tenfold overdoses. Insulins are available in different types and strengths. Check type, dose, and expiration date with another provider.
- Do not confuse Humulin with Humalog. Do not confuse Novolin with Novolog
- Use *only* insulin syringes to draw up dose. The unit markings on the insulin syringe must match the insulin's units/mL. Special syringes for doses <50 units and U–500 insulin are available. Prior to withdrawing dose, rotate vial between palms to ensure uniform solution; do not shake.
- When mixing insulins, draw regular insulin into syringe first to avoid contamination of regular insulin vial.
- Insulin should be stored in a cool place but does not need to be refrigerated. Once opened, store at room temperature. Follow manufacturer's instructions regarding storage of insulin and insulin pens before and after use.
- **SC:** Administer regular insulin within 15–30 min before a meal>
- **IV:** Do not use if cloudy, discolored, or unusually viscous. **High Alert:** Do not administer regular (concentrated) insulin U-500 IV.

- **IV Push: Diluent:** May be administered IV undiluted directly into vein or through Y-site.
- **Rate:** Administer up to 50 units over 1 min.
- **Continuous Infusion: Diluent:** May be diluted in 0.9% NaCl using polyvinyl chloride infusion bags. **Concentration:** 0.1 unit/mL to 1 unit/mL in infusion systems with the infusion fluids.
- **Rate:** Rate should be ordered by health care professional, and infusion placed on an IV pump for accurate administration.
    - Rate of administration should be decreased when serum glucose level reaches 250 mg/dL.

Metoprolol (Lopressor®)

Scope CCT

Generic Name:	**Metoprolol**
Trade Name:	Lopressor
Chemical Class:	Beta Blocker
Therapeutic Class:	Antianginal, Antihypertensive
Actions:	Blocks stimulation of $beta_1$ (myocardial)-adrenergic receptors. Does not usually affect $beta_2$ (pulmonary, vascular, uterine)-adrenergic receptor sites. **Therapeutic Effect(s):** • Decreased BP and heart rate. • Decreased frequency of attacks of angina pectoris. • Decreased rate of cardiovascular mortality and hospitalization in patients with heart failure.
Pharmacokinetics:	**Absorption:** Well absorbed after oral administration. **Distribution:** Crosses the blood-brain barrier, crosses the placenta; small amounts enter breast milk. **Metabolism and Excretion:** Mostly metabolized by the liver (primarily by CYP2D6; the CYP2D6 enzyme system exhibits genetic polymorphism); ~7% of population may be poor metabolizers and may have significantly ↑ metoprolol concentrations and an ↑ risk of adverse effects. **Half-life:** 3–7 hr. **TIME/ACTION PROFILE (cardiovascular effects)**

ROUTE	ONSET	PEAK	DURATION
PO†	15 min	unknown	6–12 hr
PO–ER	unknown	6–12 hr	24 hr
IV	immediate	20 min	5–8 hr

†Maximal effects on BP (chronic therapy) may not occur for 1 wk. Hypotensive effects may persist for up to 4 wk after discontinuation.

Indications:

- Hypertension.
- Angina pectoris.
- Prevention of MI and decreased mortality in patients with recent MI.
- Management of stable, symptomatic (class II or III) heart failure due to ischemic, hypertensive or cardiomyopathc origin (may be used with ACE inhibitors, diuretics and/or digoxin; Toprol XL only).

Contraindications/ Considerations:

Contraindicated in:

- Uncompensated HF;
- Pulmonary edema;
- Cardiogenic shock;
- Bradycardia, heart block, or sick sinus syndrome (in absence of a pacemaker).

Use Cautiously in:

- Renal impairment;
- Hepatic impairment;
- Geri: ↑ sensitivity to beta blockers; initial dose reduction recommended;
- Pulmonary disease (including asthma; $beta_1$ selectivity may be lost at higher doses);
- Diabetes mellitus (may mask signs of hypoglycemia);
- Thyrotoxicosis (may mask symptoms);
- Patients with a history of severe allergic reactions (intensity of reactions may be increased);
- Untreated pheochromocytoma (initiate only after alpha blocker therapy started);
- OB: Lactation: Pedi: Safety not established; all agents cross the placenta and may cause fetal/neonatal bradycardia, hypotension, hypoglycemia, or respiratory depression.

Precautions:

Hepatic Impairment:

Since metoprolol is extensively metabolized by the liver, blood levels are likely to increase substantially in patients with hepatic impairment. Therefore, metoprolol should be initiated at a low dose and titrated slowly according to clinical response.

Renal Impairment:
No dosage adjustment is needed.

Intermittent hemodialysis:
Supplemental doses are not needed since metoprolol is not removed by hemodialysis. However, the usual maintenance dose of metoprolol may be administered after hemodialysis.

Pregnancy Cat:	Metoprolol is classified as FDA pregnancy risk category C
Side Effects:	**CNS:** *fatigue*, *weakness*, anxiety, depression, dizziness, drowsiness, insomnia, memory loss, mental status changes, nervousness, nightmares **EENT:** blurred vision, stuffy nose **Resp:** bronchospasm, wheezing **CV:** BRADYCARDIA, HF, PULMONARY EDEMA, hypotension, peripheral vasoconstriction **GI:** constipation, diarrhea, drug-induced hepatitis, dry mouth, flatulence, gastric pain, heartburn, ↑ liver enzymes, nausea, vomiting **GU:** *erectile dysfunction*, ↓ libido, urinary frequency **Derm:** rash **Endo:** hyperglycemia, hypoglycemia **MS:** arthralgia, back pain, joint pain **Misc:** drug-induced lupus syndrome *** CAPITALS indicate life-threatening.** ***Italics* indicate most frequent.**

Administration:	**Injectable Administration** Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit. **Intravenous Administration** No dilution necessary. Monitor blood pressure, heart rate, and ECG during IV administration of metoprolol **IV: (Adults)** *MI*– 5 mg q 2 min for 3 doses, followed by oral dosing.

Supply:	**Solution for injection:** 1 mg/mL
Notes:	• **High Alert:** IV vasoactive medications are inherently dangerous. Before administering intravenously, have second practitioner independently check original order and dose calculations. • **High Alert:** Do not confuse Toprol-XL (metoprolol) with Topamax (topiramate). Do not confuse Lopressor with Lyrica. Do not confuse metoprolol tartrate with metoprolol succinate.

Milrinone (Primacor®)

Scope CCT

Generic Name:	**Milrinone**
Trade Name:	Primacor
Chemical Class:	Inotrope, vasodilator
Therapeutic Class:	Inotropics
Actions:	• Increases myocardial contractility. • Decreases preload and afterload by a direct dilating effect on vascular smooth muscle. **Therapeutic Effect(s):** Increased cardiac output (inotropic effect).
Pharmacokinetics:	**Absorption:** IV administration results in complete bioavailability. **Distribution:** Unknown**.** **Metabolism and Excretion:** 80–90% excreted unchanged by the kidneys. **Half-life:** 2.3 hr (↑ in renal impairment). **TIME/ACTION PROFILE (hemodynamic effects)**

ROUTE	ONSET	PEAK	DURATION
IV	5–15 min	unknown	3–6 hr

Indications:	Short-term treatment of HF unresponsive to conventional therapy with digoxin, diuretics, and vasodilators.
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity; • Severe aortic or pulmonic valvular heart disease; • Hypertrophic subaortic stenosis (may ↑ outflow tract obstruction). **Use Cautiously in:** • History of arrhythmias, electrolyte abnormalities, abnormal digoxin levels, or insertion of vascular catheters (↑ risk of ventricular arrhythmias);

- Renal impairment (↓ infusion rate if CCr is <50 mL/min);
- OB: Lactation: Pregnancy or lactation**.**

Precautions:

- **Hepatic Impairment**
  Specific guidelines for dosage adjustments are not available; it appears that no dosage adjustments are needed. Titrate the milrinone infusion rate to attain clinical goals.
- **Renal Impairment**
  CrCl > 50 ml/min: no dosage adjustment needed; titrate dosage to attain clinical goals.
  CrCl 41—50 ml/min: initiate maintenance IV infusion rate at 0.43 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  CrCl 31—40 ml/min: initiate maintenance IV infusion rate at 0.38 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  CrCl 21—30 ml/min: initiate maintenance IV infusion rate at 0.33 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  CrCl 11—20 ml/min: initiate maintenance IV infusion rate at 0.28 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  CrCl 6—10 ml/min: initiate maintenance IV infusion rate at 0.23 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  CrCl <= 5 ml/min: initiate maintenance IV infusion rate at 0.20 mcg/kg/min; may be titrated up to a maximum infusion rate of 0.75 mcg/kg/min.
  Intermittent hemodialysis
  It is not known whether milrinone is removed by hemodialysis. See dosage guidelines for patients with renal impairment.

Pregnancy Cat: **Milrinone** is classified as FDA pregnancy risk category C

Side Effects:

CNS: headache, tremor

CV: VENTRICULAR ARRHYTHMIAS, angina pectoris, chest pain, hypotension, supraventricular arrhythmias

CV: skin rash

GI: ↑ liver enzymes

F and E: hypokalemia

Hemat: thrombocytopenia

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:	**IV: (Adults)** *Loading dose*– 50 mcg/kg followed by *continuous infusion* at 0.5 mcg/kg/min (range 0.375–0.75 mcg/kg/min). **IV: (Infants and Children):** *Loading dose*– 50 mcg/kg over 10 min followed by *continuous infusion* at 0.5 mcg/kg/min (range 0.25–0.75 mcg/kg/min).
Supply:	**Injection:** 1 mg/mL **Premixed infusion:** 20 mg/100 mL, 40 mg/200 mL
Notes:	• **High Alert Medication:** This medication bears a heightened risk of causing significant patient harm when it is used in error. • **High Alert:** Accidental overdose of milrinone can cause patient harm or death. Have second practitioner independently check original order, dose calculations, and infusion pump settings. • **IV Push: Diluent:** Loading dose may be administered undiluted. May also be diluted in 0.9% NaCl, 0.45% NaCl, or D5W for ease of administration. **Concentration:** 1 mg/mL. • **Rate:** Administer the loading dose over 10 min. • **Continuous Infusion: Diluent:** Milrinone drawn from vials must be diluted. Dilute 10 mg (10 mL) of milrinone in 40 mL of diluent or 20 mg (20 mL) of milrinone in 80 mL of diluent. Compatible diluents include 0.45% NaCl, 0.9% NaCl, and D5W. Premixed infusions are already diluted and ready to use. Admixed solutions are stable for 72 hr at room temperature. Stability of premixed infusions based on manufacturer's expiration date. Do not use solutions that are discolored or contain particulate matter. **Concentration:** 200 mcg/mL. • **Rate:** Based on patient's weight (see Route/Dosage section). Titrate according to hemodynamic and clinical response.

Nicardipine (Cardene®)

Scope CCT

Generic Name:	**Nicardipine**
Trade Name:	Cardene
Chemical Class:	Calcium channel blockers
Therapeutic Class:	Antianginals, antihypertensives
Actions:	Inhibits the transport of calcium into myocardial and vascular smooth muscle cells, resulting in inhibition of excitation-contraction coupling and subsequent contraction. **Therapeutic Effect(s):** • Systemic vasodilation resulting in decreased BP.

- Coronary vasodilation resulting in decreased frequency and severity of attacks of angina.

Pharmacokinetics:

Absorption: Well absorbed following oral administration but extensively metabolized, resulting in ↓ bioavailability.

Distribution: Unknown.

Metabolism and Excretion: Mostly metabolized by the liver; ≤10% excreted unchanged by kidneys.

Half-life: 2–4 hr.

TIME/ACTION PROFILE (cardiovascular effects)

ROUTE	ONSET	PEAK	DURATION
IV	within min	45 min	50 hr†

†Following discontinuation.

Indications:

Management of:

- Hypertension,
- Angina pectoris,
- Vasospastic (Prinzmetal's) angina.

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity;
- Sick sinus syndrome;
- 2nd- or 3rd-degree AV block (unless an artificial pacemaker is in place);
- SBP <90 mm Hg;
- Advanced aortic stenosis.

Use Cautiously in:

- Severe hepatic impairment (dose ↓ recommended);
- Severe renal impairment (dose ↓ may be necessary);
- History of serious ventricular arrhythmias or HF;
- OB: Lactation: Pedi: Safety not established;
- Geri: Dose ↓/slower IV infusion rates recommended due to↑ risk of hypotension.

Precautions:

- **Hepatic Impairment**
  The manufacturer advises caution in patients with hepatic impairment or reduced hepatic blood flow; reduced dosage is suggested for the regular-release formulation.
- **Renal Impairment**
  No initial dosage adjustment is needed; however, careful dose titration is advised when treating renally impaired patients. Begin with the initial adult dosage, and cautiously adjust the nicardipine dosage based on clinical response.

  Intermittent hemodialysis
  Nicardipine is not significantly removed by hemodialysis.

Pregnancy Cat:	**Nicardipine** is classified as FDA pregnancy risk category C
Side Effects:	**CNS:** abnormal dreams, anxiety, confusion, dizziness, drowsiness, headache, jitteriness, nervousness, psychiatric disturbances, weakness **EENT:** blurred vision, disturbed equilibrium, epistaxis, tinnitus **Resp:** cough, dyspnea, shortness of breath **CV:** ARRHYTHMIAS, HF, *peripheral edema*, bradycardia, chest pain, hypotension, palpitations, syncope, tachycardia **GI:** ↑ liver function tests, anorexia, constipation, diarrhea, dry mouth, dysgeusia, dyspepsia, nausea, vomiting **GU:** dysuria, nocturia, polyuria, sexual dysfunction, urinary frequency **Derm:** dermatitis, erythema multiforme, flushing, ↑ sweating, photosensitivity, pruritus/urticaria, rash **Endo:** gynecomastia, hyperglycemia **Hemat:** anemia, leukopenia, thrombocytopenia **Metabolic:** weight gain **MS:** joint stiffness, muscle cramps **Neuro:** paresthesia, tremor **Misc:** STEVENS-JOHNSON SYNDROME, gingival hyperplasia * CAPITALS indicate life-threatening. *Italics* indicate most frequent.
Administration:	**IV: (Adults)** *Substitute for PO nicardipine*– if PO dose is 20 mg q 8 hr, then infusion rate is 0.5 mg/hr; if PO dose is 30 mg q 8 hr, then infusion rate is 1.2 mg/hr; if PO dose is 40 mg q 8 hr, then infusion rate is 2.2 mg/hr. *Patients not receiving PO nicardipine*– initiate therapy at 5 mg/hr, may be increased by 2.5 mg q 5–15 min as needed (up to 15 mg/hr).
Supply:	**Injection:** 2.5 mg/mL **Premixed infusion:** 20 mg/200 mL D5W or 0.9% NaCl
Notes:	• Do not confuse Cardene with Cardizem. Do not confuse nicardipine with nifedipine or nimodipine. • **Continuous Infusion: Diluent:** Dilute each 25-mg ampule with 240 mL of D5W, D5/0.45% NaCl, D5/0.9% NaCl, 0.45% NaCl, or 0.9% NaCl. Infusion is stable for 24 hr at room temperature. **Concentration:** 0.1 mg/mL. • **Rate:** Titrate rate according to BP response. Administer through large peripheral veins or central veins to reduce risk of venous thrombosis, phlebitis, local irritation, swelling, extravasation, and vascular impairment. Change infusion site every 12 hours to minimize risk of peripheral venous irritation.

Norepinephrine (Levophed®)

Scope C3IFT | CCT

Generic Name:	**Norepinephrine**
Trade Name:	Levophed®
Chemical Class:	Vasopressor
Therapeutic Class:	Vasopressor
Actions:	Mechanism of Action: Norepinephrine acts predominantly on alpha-adrenergic receptors to produce constriction of resistance and capacitance vessels, thereby increasing systemic blood pressure and coronary artery blood flow. Norepinephrine also acts on beta1-receptors, although quantitatively less than either epinephrine or isoproterenol. In relatively lower doses, the cardiac-stimulant effect of norepinephrine is predominant; with larger doses, the vasoconstrictor effect predominates.Similar to epinephrine, norepinephrine has direct agonist effects on effector cells that contain alpha- and beta-receptors. As with other catecholamines, the intracellular action of norepinephrine is mediated via cyclic adenosine monophosphate (cAMP), the production of which is augmented by beta stimulation and attenuated by alpha stimulation.The primary pharmacodynamic effects of norepinephrine are cardiac stimulation, particularly at lower doses, and vasoconstriction, which tends to predominate with moderate to higher doses of the drug. Metabolic effects observed with epinephrine, such as glycogenolysis, inhibition of insulin release, and lipolysis, also occur with norepinephrine but are much less pronounced.The hemodynamic consequences of norepinephrine's cardiovascular stimulation include increases in systolic, diastolic, and pulse pressures. Cardiac output is generally unaffected, although it can be decreased, and total peripheral resistance is also elevated. The elevation in resistance and pressure result in reflex vagal activity, which slows the heart rate and increases stroke volume. The elevation in vascular tone or resistance reduces blood flow to the major abdominal organs as well as to skeletal muscle. As with epinephrine, however, coronary blood flow is substantially increased secondary to the indirect effects of alpha stimulation. Therefore, unlike epinephrine, norepinephrine does not significantly increase myocardial oxygen consumption, except in patients with variant angina who are hyperresponsive to alpha stimulation.
Pharmacokinetics:	**Absorption:** IV administration results in complete bioavailability**.** **Distribution:** Concentrates in sympathetic nervous tissue. Does not cross the blood-brain barrier but readily crosses the placenta. **Metabolism and Excretion:** Taken up and metabolized rapidly by sympathetic nerve endings. **Half-life:** Unknown**.** **TIME/ACTION PROFILE (effects on BP)**

ROUTE	ONSET	PEAK	DURATION
IV	immediate	rapid	1–2 min

Indications:	Produces vasoconstriction and myocardial stimulation, which may be required after adequate fluid replacement in the treatment of severe hypotension and shock.
Contraindications/ Considerations:	**Contraindicated in:** • Vascular, mesenteric, or peripheral thrombosis;

- OB: ↓ uterine blood flow;
- Hypoxia;
- Hypercarbia;
- Hypotension secondary to hypovolemia (without appropriate volume replacement);
- Hypersensitivity to bisulfites.

Use Cautiously in:

- Hypertension;
- Concurrent use of MAO inhibitors, tricyclic antidepressants, or cyclopropane or halothane anesthetics;
- Hyperthyroidism;
- Cardiovascular disease;
- Lactation: Safety not established

Precautions:

Hepatic Impairment

Specific guidelines for dosage adjustments are not available; however, the rate of metabolism of norepinephrine may be decreased in individual patients with hepatic impairment. Titrate the norepinephrine infusion rate to attain clinical goals.

Renal Impairment

Specific guidelines for dosage adjustments are not available; it appears that no dosage adjustments are needed. Titrate the norepinephrine dosage to attain clinical goals.

Intermittent hemodialysis:
It is unknown whether norepinephrine is dialyzable. Titrate the norepinephrine infusion rate to attain clinical goals.

Pregnancy Cat: Norepinephrine is classified as FDA pregnancy risk category C

Side Effects: **Severe**

- arrhythmia exacerbation
- pulmonary edema
- bradycardia
- lactic acidosis
- tissue necrosis
- anaphylactic shock

Moderate

- photophobia
- hypertension
- sinus tachycardia
- premature ventricular contractions (PVCs)
- angina
- dyspnea
- palpitations
- ST-T wave changes
- hypovolemia
- hypoxia

Administration:

NOTE: Volume depletion should always be corrected before initiation of vasopressor therapy. However, in an emergency, when intraaortic pressures must be maintained to prevent cerebral or coronary artery ischemia, norepinephrine can be administered prior to and concurrently with volume replacement therapy.

NOTE: Norepinephrine is available commercially only as the bitartrate salt, although the dosage is expressed in terms of norepinephrine base (2 mg norepinephrine bitartrate equals 1 mg norepinephrine base).

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration**.**

Intravenous Administration

Administer by intravenous infusion.

Monitor blood pressure every 2—3 minutes until stabilized and then every 5 minutes. ECG should be continuously monitored.

Do not administer into the veins of the legs in elderly patients.

Avoid extravasation (see Precautions). If extravasation occurs, infiltrate the site as soon as possible with 10—15 ml of NS containing 5—10 mg of phentolamine for adults (see Phentolamine Dosage). Use a syringe with a fine hypodermic needle and liberally infiltrate throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and noticeable local hyperemic changes if the area is infiltrated within 12 hours of extravasation. For prevention of extravasation, phentolamine (10 mg) may be added to each 1000 ml of solution containing norepinephrine.

Dilution:

The concentrate for injection must be diluted prior to administration. Fluids containing dextrose offer protection against loss of potency due to oxidation; therefore, 5% dextrose in water (D5W) or 5% percent dextrose and sodium chloride (D5NS) are generally the preferred diluents. Although the manufacturer states that norepinephrine should not be diluted in normal saline (NS) alone, available data support the stability of norepinephrine in NS at concentrations up to 16 mcg/ml.

The manufacturer recommends diluting 4 mg norepinephrine in 1000 ml of D5W for a concentration of 4 mcg/ml. However, a more commonly used dilution in clinical practice is 4 mg norepinephrine in 250 ml of D5W injection for a concentration of 16 mcg/ml. In fluid-restricted patients, concentrations up to 32 mcg/ml have been used.

Intravenous infusion:

Infuse IV preferably into the antecubital vein of the arm using an infusion pump or other device to control the flow rate. The femoral vein may also be used. Do not use a catheter tie-in technique because the obstruction to blow flow around the tubing may lead to stasis and increased local concentration of norepinephrine. Rate should be titrated according to patient response.

Observe IV infusion site frequently during administration. If blanching along the vein occurs, change infusion site. Care should be taken to avoid extravasation because norepinephrine can cause local necrosis.

For the treatment of acute hypotension, cardiogenic shock, sepsis, or septic shock.

Intravenous dosage

Adults

Initially, up to 8 to 12 mcg/minute, as an IV infusion, titrated to desired hemodynamic response (usually to maintain systolic BP of 80 to 100 mm Hg). Infusions are typically initiated and titrated in increments of 0.02 mcg/kg/minute (or more in emergency cases). Usual maintenance dose is 2 to 4 mcg/minute. Individual response is highly variable. Patients with refractory shock may require dosages of 8 to 30 mcg/minute. There are rare situations in which much larger doses (as high as 68 mg/day or 47 mcg/minute) may be necessary if the patient remains hypotensive; however, rule out hidden blood volume depletion. One trial limited infusions to a maximum of 0.19 mcg/kg/minute, then added additional agents for the treatment of shock. Septic shock clinical practice guidelines recommend norepinephrine as the first-line vasopressor. Target a mean arterial pressure (MAP) of 65 mmHg initially. Titrate to an endpoint reflecting perfusion; reduce rate or discontinue the vasopressor if worsening hypotension or arrhythmias occur. Compared to other vasopressors, norepinephrine increases MAP with little change in heart rate and less increase in stroke volume. Discontinuation of therapy should occur when adequate blood pressure and tissue perfusion are maintained following gradual tapering of the infusion rate. NOTE: In general, norepinephrine should not be used for treating hypotension during anesthesia; the benefits and risks of using norepinephrine should be evaluated.

Infants†, Children†, and Adolescents†

0.1 mcg/kg/minute IV initially, then titrate upward to attain hemodynamic goals (Usual Max: 2 mcg/kg/minute IV). When discontinuing norepinephrine, reduce the infusion rate gradually; avoid abrupt withdrawal.

Neonates†

0.2 to 0.5 mcg/kg/minute IV initially titrated upward every 30 minutes to attain clinical goals was used in an observational study of 22 neonates (gestational age older than 35 weeks) with hypotension due to septic shock refractory to fluid resuscitation and dopamine or dobutamine infusion. The norepinephrine infusion rate required to correct hypotension ranged from 0.2 to 2 mcg/kg/minute (mean 0.5 mcg/kg/minute), and the individual maximum infusion rate to sustain normal systolic blood pressure ranged from 0.2 to 7.1 mcg/kg/minute. A dose range of 0.1 to 2 mcg/kg/minute is recommended by the Pediatric Advanced Life Support guidelines. When discontinuing norepinephrine, reduce the infusion rate gradually; avoid abrupt withdrawal.

†Indicates off-label use

Supply: Levophed/Norepinephrine/Norepinephrine Bitartrate Intravenous Inj Sol: 1mg, 1mL

Notes:

- ***BOXED WARNING***: Extravasation, geriatric, peripheral vascular disease, tissue necrosis.Caution should be observed to avoid extravasation of norepinephrine during intravenous administration. Check the infusion site frequently for free-flow. Peripheral vasoconstriction or ischemia, tissue necrosis, and/or gangrene in the surrounding area can occur following extravasation. Blanching along the course of the infused vein, sometimes without obvious extravasation, has been attributed to vasa vasorum constriction with increased permeability of the vein wall, permitting some leakage. This also may progress on rare occasions to superficial slough, particularly during infusion into leg veins in geriatric patients or in those suffering from obliterative peripheral vascular disease. Hence, if blanching occurs, consideration should be given to the advisability of changing the infusion site at intervals to allow the effects of local vasoconstriction to subside. If extravasation occurs, the affected area should be infiltrated as soon as possible, to prevent necrosis, using a normal saline solution containing phentolamine, injecting liberally throughout the ischemic area using a fine hypodermic needle. The ischemic area may be identified by a cool, hard, and pallid appearance. Sympathetic blockade with phentolamine causes immediate and noticeable local hyperemic changes if the area is infiltrated within 12 hours of extravasation. The phentolamine antidote should be given as soon as possible after the extravasation is observed.

- Use with **cyclopropane** or **halothane anesthesia** , **cardiac glycosides** , **doxapram** , or local use of **cocaine** may result in ↑ myocardial irritability.
- Use with **MAO inhibitors** , **methyldopa** , **doxapram** , or **tricyclic antidepressants** may result in severe hypertension.

- **Alpha-adrenergic blockers** can prevent pressor response.
- **Beta blockers** may exaggerate hypertension or block cardiac stimulation.
- Concurrent use with **ergot alkaloids** (**ergotamine** , **methylergonovine** , or **oxytocin** may result in enhanced vasoconstriction and hypertension.

Phenobarbital (Ancalixir®Luminal®)

Scope CCT

Generic Name:	**Phenobarbital**
Trade Name:	**Ancalixir®Luminal®**
Chemical Class:	Barbiturates
Therapeutic Class:	Anticonvulsants, sedative/hypnotics
Actions:	• Produces all levels of CNS depression. • Depresses the sensory cortex, decreases motor activity, and alters cerebellar function. • Inhibits transmission in the nervous system and raises the seizure threshold. • Capable of inducing (speeding up) enzymes in the liver that metabolize drugs, bilirubin, and other compounds. **Therapeutic Effect(s):** • Anticonvulsant activity. • Sedation.
Pharmacokinetics:	**Absorption:** Absorption is slow but relatively complete (70–90%). **Distribution:** Unknown. **Metabolism and Excretion:** 75% metabolized by the liver, 25% excreted unchanged by the kidneys. **Half-life: Neonates:** 1.8–8.3 days; Infants: 0.8–5.5 days; Children: 1.5–3 days; Adults: 2–6 days. **TIME/ACTION PROFILE (sedation†)**

ROUTE	ONSET	PEAK	DURATION
IM, subcut	10–30 min	unknown	4–6 hr
IV	5 min	30 min	4–6 hr

Indications:	• Anticonvulsant in tonic-clonic (grand mal), partial, and febrile seizures in children. • Preoperative sedative and in other situations in which sedation may be required. • Hypnotic (short-term).

Unlabeled Use(s):
Prevention/treatment of hyperbilirubinemia in neonates.

Contraindications/ Considerations:

Contraindicated in:

- **Hypersensitivity;**
- **Comatose patients or those with pre-existing CNS depression;**
- **Severe respiratory disease with dyspnea or obstruction;**
- **Uncontrolled severe pain;**
- **Known alcohol intolerance (elixir only);**
- **Lactation: Discontinue drug or bottle feed.**

Use Cautiously in:

- Hepatic dysfunction;
- Severe renal impairment;
- History of suicide attempt or drug abuse;
- Hypnotic use should be short-term. Chronic use may lead to dependence;
- OB: Chronic use during pregnancy results in drug dependency in the infant; may result in coagulation defects and fetal malformation; acute use at term may result in respiratory depression in the newborn;
- Geri: Initial dose ↓ recommended

Precautions:

- **Hepatic Impairment**
  Modify initial dose depending on degree of hepatic impairment; no quantitative recommendations are available. Initiate dose cautiously and adjust based on clinical response and serum concentrations. Initiate dose cautiously and adjust based on clinical response and serum concentrations.
- **Renal Impairment**
  CrCl >= 10 mL/minute: No dosage adjustment needed.
  CrCl < 10 mL/minute: In adult patients, extend interval to every 12 to 16 hours. In pediatric patients, decrease dose by 50% and administer every 24 hours.

  Intermittent hemodialysis:
  Phenobarbital is efficiently removed by hemodialysis. Dosage schedules should be adjusted so that the timing of a normally administered dosage is given after the hemodialysis session.

Pregnancy Cat: **Phenobarbital** is classified as FDA pregnancy risk category D

Side Effects:
CNS: *hangover*, delirium, depression, drowsiness, excitation, lethargy, vertigo
Resp: respiratory depression**IV:** LARYNGOSPASM, bronchospasm
CV: IV: hypotension
GI: constipation, diarrhea, nausea, vomiting
Derm: photosensitivity, rashes, urticaria
Local: phlebitis at IV site
MS: arthralgia, myalgia, neuralgia
Misc: HYPERSENSITIVITY REACTIONS INCLUDING ANGIOEDEMA AND SERUM SICKNESS, physical dependence, psychological dependence

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Status Epilepticus

IV: (Adults and Children >1 mo): 15–18 mg/kg in a single or divided dose, maximum loading dose 20 mg/kg.

IV: Neonates 15–20 mg/kg in a single or divided dose.

Maintenance Anticonvulsant

IV: PO: (Adults and Children >12 yr): 1–3 mg/kg/day as a single dose or 2 divided doses.

IV: PO: (Children 5–12 yr): 4–6 mg/kg/day in 1–2 divided doses.

IV: PO: (Children 1–5 yr): 6–8 mg/kg/day in 1–2 divided doses.

IV: PO: Infants 5–6 mg/kg/day in 1–2 divided doses.

IV: PO: Neonates 3–4 mg/kg/day once daily, may need to increase up to 5 mg/kg/day by 2nd week of therapy.

Supply: **Injection:** 65 mg/mL, 130 mg/mL

Notes:

- Monitor respiratory status, pulse, and BP and signs and symptoms of angioedema (swelling of lips, face, throat, dyspnea) frequently in patients receiving phenobarbital IV. Equipment for resuscitation and artificial ventilation should be readily available. Respiratory depression is dose-dependent.
- **Geri:** Elderly patients may react to phenobarbital with marked excitement, depression, and confusion. Monitor for these adverse reactions.
- Do not confuse phenobarbital with pentobarbital
- **IV:** Doses may require 15–30 min to reach peak concentrations in the brain. Administer minimal dose and wait for effectiveness before administering 2nd dose to prevent cumulative barbiturate-induced depression.
- **IV Push: Diluent:** Reconstitute sterile powder for IV dose with a minimum of 3 mL of sterile water for injection. Dilute further with 10 mL of sterile water. Do not use solution that is not absolutely clear within 5 min after reconstitution or that contains a precipitate. Discard powder or solution that has been exposed to air for longer than 30 min.
    - Solution is highly alkaline; avoid extravasation, which may cause tissue damage and necrosis. If extravasation occurs, injection of 5% procaine solution into affected area and application of moist heat may be ordered.
- **Concentration:** 130 mg/mL (undiluted).

- **Rate:** Do not inject IV faster than 1 mg/kg/min with a maximum of 30 mg over 1 min in infants and children and 60 mg over 1 min in adults. Titrate slowly for desired response. Rapid administration may result in respiratory depression.

Phenylephrine (Neo-synephrine® Vazculep®)

Scope CCT

Generic Name:	**Phenylephrine**
Trade Name:	**Neo-synephrine® Vazculep®)**
Chemical Class:	Adrenergics, alpha adrenergic agonists, vasopressors
Therapeutic Class:	Vasopressor
Actions:	Constricts blood vessels by stimulating alpha-adrenergic receptors. **Therapeutic Effect(s):** Increased BP.
Pharmacokinetics:	**Absorption:** Well absorbed from IM sites. IV administration results in complete bioavailability. **Distribution:** Highly distributed into organs and tissues. **Metabolism and Excretion:** Metabolized by the liver into inactive metabolites. **Half-life:** 2.5 hr**.** **TIME/ACTION PROFILE (vasopressor effects)**

ROUTE	ONSET	PEAK	DURATION
IV	immediate	unknown	15–20 min
IM	10–15 min	unknown	0.5–2 hr
Subcut	10–15 min	unknown	50–60 min

Indications:	• Management of hypotension associated with shock that may persist after adequate fluid replacement. • Management of hypotension associated with anesthesia.
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity to bisulfites. **Use Cautiously in:** • HF, coronary artery disease, or peripheral arterial disease; • OB: Lactation: Safety not established.

Precautions:

- **Hepatic Impairment**
  Specific guidelines for dosage adjustments in hepatic impairment are not available. For patients with liver cirrhosis, initiate dosing in the recommended dose range; however, due to decreased responsiveness, higher doses may be needed.
- **Renal Impairment**
  Specific guidelines for dosage adjustments in renal impairment are not available. For patients with end stage renal disease, consider using lower doses.

Pregnancy Cat: **Phenylephrine** is classified as FDA pregnancy risk category C

Side Effects:
CNS: blurred vision, headache, insomnia, nervousness, tremor
Resp: dyspnea
CV: ARRHYTHMIAS, bradycardia, chest pain, hypertension, ischemia, tachycardia
Derm: pruritis
GI: epigastric pain, nausea, vomiting
Local: phlebitis, sloughing at IV sites
* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Hypotension

SC: IM: (Adults) 2–5 mg.

SC: IM: Children 0.1 mg/kg/dose q 1–2 hr as needed, maximum dose 5 mg.

IV: (Adults) 0.2 mg (range 0.1–0.5 mg), may be repeated q 10–15 min *or* as an infusion at 100–180 mcg/min initially, 40–60 mcg/min maintenance.

IV: Children 5–20 mcg/kg/dose q 10–15 min as needed or 0.1–0.5 mcg/kg/min infusion, titrate to effect.

Supply: **Injection:** 10 mg/mL

Notes:	• **High Alert Medication:** This medication bears a heightened risk of causing significant patient harm when it is used in error. • **High Alert:** Patient harm and fatalities have occurred from medication errors with phenylephrine. Prior to administration, have second practitioner independently check original order, dose calculations, concentration, route of administration and infusion pump settings. • **IV:** Blood volume depletion should be corrected, if possible, before initiation of IV phenylephrine. • **IV Push: Diluent:** Dilute each 1 mg with 9 mL of sterile water for injection or D5W. • **Rate:** Administer each single dose over 1 min. • **Continuous Infusion: Diluent:** Dilute 10 mg in 250 or 500 mL of D5W or 0.9% NaCl. **Concentration:** 125,000 or 150,000 solution, respectively. • **Rate:** Titrate rate according to patient response. Infuse via infusion pump to ensure accurate dose rate.

Phenytoin (Dilantin®, Phenytek® ,Tremytoine®)

Scope | | **CCT**

Generic Name:	**Phenytoin**
Trade Name:	**Dilantin®, Phenytek® ,Tremytoine®**
Chemical Class:	Hydantoins
Therapeutic Class:	Antiarrhythmics (group IB) Anticonvulsants
Actions:	• Limits seizure propagation by altering ion transport. • May also decrease synaptic transmission. • Antiarrhythmic properties as a result of shortening the action potential and decreasing automaticity. **Therapeutic Effect(s):** • Diminished seizure activity. • Termination of ventricular arrhythmias.
Pharmacokinetics:	**Absorption:** Absorbed slowly from the GI tract. Bioavailability differs among products; the Dilantin and Phenytek preparations are considered to be "extended" products. Other products are considered to be prompt release. **Distribution:** Distributes into CSF and other body tissues and fluids. Enters breast milk; crosses the placenta, achieving similar maternal/fetal levels. Preferentially distributes into fatty tissue. **Protein Binding:** Adults 90–95%; ↓ protein binding in neonates (up to 20% free fraction available), infants (up to 15% free), and patients with hyperbilirubinemia, hypoalbuminemia, severe renal dysfunction or uremia. **Metabolism and Excretion:** Mostly metabolized by the liver; minimal amounts excreted in the urine. **Half-life:** 22 hr (range 7–42 hr). **TIME/ACTION PROFILE (anticonvulsant effect)**

ROUTE	ONSET	PEAK	DURATION
IV	0.5–1 hr (1 wk)	rapid	12–24 hr

***() = time required for onset of action without a loading dose**

Indications:

Treatment/prevention of tonic-clonic (grand mal) seizures and complex partial seizures.

Unlabeled Use(s):

- As an antiarrhythmic, particularly for ventricular arrhythmias associated with digoxin toxicity, prolonged QT interval, and surgical repair of congenital heart diseases in children.
- Management of neuropathic pain, including trigeminal neuralgia.

Contraindications/ Considerations:

Contraindicated in:

- Hypersensitivity;
- Hypersensitivity to propylene glycol (phenytoin injection only);
- Alcohol intolerance (phenytoin injection and liquid only);
- Sinus bradycardia, sinoatrial block, 2nd- or 3rd-degree heart block, or Stokes-Adams syndrome (phenytoin injection only);
- Concurrent use of delavirdine

Use Cautiously in:

- All patients (may ↑ risk of suicidal thoughts/behaviors);
- Hepatic or renal disease (↑ risk of adverse reactions; dose reduction recommended for hepatic impairment);
- Patients with severe cardiac or respiratory disease (use of IV phenytoin may result in an ↑ risk of serious adverse reactions);
- OB: ↑ risk of congenital anomalies; ↑ risk of hemorrhage in newborn if used at term; use with extreme caution;
- Lactation: Safety not established;
- Pedi: Suspension contains sodium benzoate, a metabolite of benzyl alcohol that can cause potentially fatal gasping syndrome in neonates;
- Geri: Use of IV phenytoin may result in an ↑ risk of serious adverse reactions.

Exercise Extreme Caution in:

Patients positive for HLA-B*1502 allele (unless exceptional circumstances exist where benefits clearly outweigh the risks).

Precautions:

- **Hepatic Impairment**
  Dosage adjustments may be required based on serum phenytoin concentrations and clinical response. Phenytoin is primarily metabolized in the liver. Patients with hepatic disease may have an increased fraction of unbound ('free') phenytoin.
- **Renal Impairment**
  Dosage adjustments may be required based on serum phenytoin concentrations and clinical response. Patients with renal disease may have an increased fraction of unbound ('free') phenytoin.

  Intermittent hemodialysis

Phenytoin is not significantly removed during a standard hemodialysis session; therefore, supplemental dosing after hemodialysis is not necessary.

Pregnancy Cat: **Phenytoin** is classified as FDA pregnancy risk category D

Side Effects:

Most listed are for chronic use of phenytoin

CNS: SUICIDAL THOUGHTS, *ataxia*, agitation, confusion, dizziness, drowsiness, dysarthria, dyskinesia, extrapyramidal syndrome, headache, insomnia, vertigo, weakness

EENT: *diplopia*, *nystagmus*

CV: *hypotension (↑ with IV phenytoin)*, tachycardia

GI: ACUTE HEPATIC FAILURE, *gingival hyperplasia*, *nausea*, constipation, drug-induced hepatitis, vomiting

Derm: STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, *hypertrichosis*, *rash*, exfoliative dermatitis, pruritus, purple glove syndrome

Hemat: AGRANULOCYTOSIS, APLASTIC ANEMIA, leukopenia, megaloblastic anemia, thrombocytopenia

MS: osteomalacia, osteoporosis

Misc: DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS), fever, lymphadenopathy

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Anticonvulsant

IV: (Adults) *Status epilepticus loading dose*– 15–20 mg/kg. Rate not to exceed 25–50 mg/min. *Maintenance dose*– same as PO dosing above.

IV: Children *Status epilepticus loading dose*– 15–20 mg/kg at 1–3 mg/kg/min. *Maintenance dose*– same as PO dosing above.

Supply: **Injection:** 50 mg/mL

Notes:

BOXED WARNING

Adams-Stokes syndrome, AV block, bradycardia, bundle-branch block, cardiac arrhythmias, cardiac disease, coronary artery disease, heart failure, hypotension, infusion-related reactions, intravenous administration

Phenytoin injection is contraindicated in patients with sinus bradycardia, sino-atrial block, second or third degree AV block, and Adams-Stokes syndrome because of the effects of the drug on ventricular automaticity. Intravenous phenytoin should not be used in patients with other cardiac conduction abnormalities (e.g., bundle-branch block) and should be used with caution in any patient with cardiac disease, such as cardiac arrhythmias, congestive heart failure, or coronary artery disease, because symptoms may be potentiated or exacerbated. In addition, FDA-approved labeling for parenteral phenytoin contains a boxed warning that highlights infusion-related reactions, specifically cardiovascular risks, associated with rapid intravenous administration rates. Severe cardiovascular reactions have occurred, including bradycardia, heart block, ventricular tachycardia, and ventricular fibrillation, which have resulted in asystole, cardiac arrest, and death in some cases. The rate of intravenous administration is critically important to avoid or limit adverse events; do not exceed recommended infusion rates. In elderly or debilitated patients, some experts suggest infusing IV no faster than 25 mg/minute; consider slower infusion rates if concurrent cardiac disease is present. Though the manufacturer recommends a pediatric infusion rate of 1 to 3 mg/kg/minute (not to exceed 50 mg/minute) most experts recommend not exceeding a rate of 1 mg/kg/minute in any pediatric patient. Hypotension may occur, especially after high doses are given at high rates of administration. Although the risk of cardiovascular toxicity is increased with rapid intravenous administration, cardiac events have also been reported at or below the recommended infusion rates. Reactions to parenteral phenytoin occur more often in elderly or debilitated patients, children (particularly infants), those who are critically ill, or those with pre-existing hypotension or severe myocardial insufficiency. Careful cardiac and respiratory monitoring is required during and after intravenous phenytoin administration. A reduction in the rate of administration or discontinuation of the drug may be necessary if cardiac reactions occur. Some cardiac effects are thought to be secondary to the propylene glycol (PEG) diluent of the parenteral product.

- **IV:** Slight yellow color will not alter solution potency. If refrigerated, may form precipitate, which dissolves after warming to room temperature. Discard solution that is not clear.
    - To prevent precipitation and minimize local venous irritation, follow infusion with 0.9% NaCl through the same needle or catheter. Avoid extravasation; phenytoin is caustic to tissues; may lead to purple glove syndrome. Monitor infusion site closely.
- **IV Push:** Administer undiluted.
- **Rate:** Administer at a rate not to exceed 50 mg over 1 min in adults or 1–3 mg/kg/min in neonates. Rapid administration may result in severe hypotension, cardiovascular collapse, or CNS depression.
- **Intermittent Infusion: Diluent:** Administer by mixing with no more than 50 mL of 0.9% NaCl. **Concentration:** 1–10 mg/mL. Administer immediately following admixture. Use tubing with a 0.45- to 0.22-micron in-line filter.

- **Rate:** Complete infusion within 1 hr at a rate not to exceed 50 mg/min. In patients who may develop hypotension, patients with cardiovascular disease, or geriatric patients maximum rate of 25 mg/min [may be as low as 5–10 mg/min]. Maximum rate in neonates is 1–3 mg/kg/min. Monitor cardiac function and BP throughout infusion.

Potassium Chloride

Scope | **CCT**

Generic Name:	**Potassium Chloride**
Trade Name:	
Chemical Class:	Electrolyte
Therapeutic Class:	mineral and electrolyte replacements/supplements
Actions:	• Maintain acid-base balance, isotonicity, and electrophysiologic balance of the cell. • Activator in many enzymatic reactions; essential to transmission of nerve impulses; contraction of cardiac, skeletal, and smooth muscle; gastric secretion; renal function; tissue synthesis; and carbohydrate metabolism. **Therapeutic Effect(s):** • Replacement. • Prevention of deficiency.
Pharmacokinetics:	**Absorption:** Well absorbed following oral administration. **Distribution:** Enters extracellular fluid; then actively transported into cells. **Metabolism and Excretion:** Excreted by the kidneys. **Half-life:** Unknown. **TIME/ACTION PROFILE (increase in serum potassium levels)**

ROUTE	ONSET	PEAK	DURATION
PO	unknown	1–2 hr	unknown
IV	rapid	end of infusion	unknown

Indications:	• Treatment/prevention of potassium depletion. • Arrhythmias due to digoxin toxicity.
Contraindications/ Considerations:	**Contraindicated in:** • Hyperkalemia • Severe renal impairment • Untreated Addison's disease • Severe tissue trauma • Hyperkalemic familial periodic paralysis

- Potassium acetate injection contains aluminum, which may become toxic with prolonged use to high risk groups (renal impairment, premature neonates).

Use Cautiously in:

- Cardiac disease
- Renal impairment
- Hypomagnesemia (may make correction of hypokalemia more difficult)
- Patients receiving potassium-sparing drugs.

Precautions:

Hepatic Impairment:

Dosage should be modified depending on clinical response. Monitor serum potassium levels.

Renal Impairment:

Dosage should be modified depending on clinical response and degree of renal impairment, but no quantitative recommendations are available. Monitor serum potassium levels and renal function carefully to avoid development of hyperkalemia.

Pregnancy Cat: Potassium Chloride is classified as FDA pregnancy risk category C

Side Effects:

CNS: confusion, restlessness, weakness

CV: ARRHYTHMIAS, ECG changes

Local: irritation at IV site

Neuro: paralysis, paresthesia

* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

Normal Daily Requirements

IV: (Adults) 40–80 mEq/day.

IV: Children 2–3 mEq/kg/day.

IV: Neonates 2–6 mEq/kg/day.

Treatment of Hypokalemia

IV: (Adults) 10–20 mEq/dose (maximum: 40 mEq/dose) to infuse over 2–3 hr (maximum infusion rate: 40 mEq/hr).

IV: (Neonates, Infants and Children): 0.5–1 mEq/kg/dose (maximum 30 mEq/dose) as an infusion to infuse at 0.3–0.5 mEq/kg/hr (maximum infusion rate 1 mEq/kg/hr).

Supply: **Potassium Chloride**

Concentrate for injection: 0.1 mEq/mL in 10-mEq ampules and vials, 0.2 mEq/mL in 10- and 20-mEq ampules and vials, 0.3 mEq/mL in 30-mEq ampules and vials, 0.4 mEq/mL in 20- and 40-mEq ampules and vials, 1.5 mEq/mL, 2 mEq/mL, 3 mEq/mL

Solution for IV infusion: 10 mEq/L in various dextrose and saline solutions in 250-, 500-, and 100-mL containers, 20 mEq/L in dextrose/saline/LRs in 250-, 500-, and 100-mL containers, 30 mEq/L in various dextrose and saline solutions in 250-, 500-, and 100-mL containers, 40 mEq/L in various dextrose and saline solutions in 250-, 500-, and 100-mL containers

Notes:

- **Continuous Infusion: High Alert:** Do not administer concentrations of ≥1.5 mEq/mL undiluted; fatalities have occurred. Concentrated products have black caps on vials or black stripes above constriction on ampules and are labeled with a warning about dilution requirement. Each single dose must be diluted and thoroughly mixed in 100–1000 mL of IV solution. Usually limited to 80 mEq/L via peripheral line (200 mEq/L via central line).
- Concentrations of 0.1 and 0.4 mEq/mL are intended for administration via calibrated infusion device and do not require dilution.
- **Rate: High Alert:** Infuse slowly, at a rate up to 10 mEq/hr in adults or 0.5 mEq/kg/hr in children in general care areas. Check hospital policy for maximum infusion rates (maximum rate in monitored setting 40 mEq/hr in adults or 1 mEq/kg/hr in children). Use an infusion pump.
- **Solution Compatibility:** May be diluted in dextrose, saline, Ringer's solution, LR, dextrose/saline, dextrose/Ringer's solution, and dextrose/LR combinations. Commercially available premixed with many of the above IV solutions.

Procainamide (Pronestyl®, Procanbid®)

Scope | CCT

Generic Name:	**Procainamide**
Trade Name:	Pronestyl®, Procanbid®
Chemical Class:	
Therapeutic Class:	class IA antiarrhythmic
Actions:	Procainamide inhibits the influx of sodium through membrane pores. Procainamide exerts its effects on 'fast' channels of the myocardial cell membrane, prolonging the

	recovery period after repolarization. The effective refractory period and the action potential duration in the atria, ventricles, and His-Purkinje system are prolonged. The effective refractory period is increased more than the action potential duration; therefore, the myocardium remains refractory even after the resting membrane potential has been restored. The drug decreases myocardial automaticity, excitability, conduction velocity, and possibly contractility. Procainamide also exhibits anticholinergic properties that may modify its myocardial effects, however these actions are less pronounced than for either quinidine or disopyramide. The net effect of procainamide is to suppress ectopy in atrial and ventricular tissue. Because nodal tissue is more dependent on calcium influx, procainamide has little use in arrhythmias of nodal origin. Clinically, procainamide is used mainly in the treatment of atrial fibrillation and/or flutter, for which it is generally considered a second-line agent after quinidine. Procainamide is an alternative antiarrhythmic for the treatment of stable ventricular tachycardia in patients with preserved left ventricular function.
Pharmacokinetics:	Onset 10-30 min. Peak 15-60 min. Duration 3-6 Hr. $t_{½}$ =.
Indications:	• Used for ventricular tachycardia. Off label uses with additional considerations include WPW, atrial fibrillation/flutter, paroxysmal atrial tachycardia
Contraindications/ Considerations:	• **Cardiogenic shock, hemorrhagic shock, hypotension, shock, AV block, bradycardia, bundle-branch block, QT prolongation, hypocalcemia, hypokalemia, torsade de pointes, ventricular dysfunction**
Precautions:	**Atrial fibrillation, atrial flutter** It is recommended that patients with atrial flutter or atrial fibrillation be adequately digitalized or have undergone cardioversion prior to therapy with procainamide in order to avoid enhancement of AV conduction and acceleration of ventricular rate. Digitalization in these patients reduces but does not eliminate the possibility of ventricular rate increases. **Hepatic Impairment** Although no specific guidelines are available, dosage reduction may be needed in individual patients with hepatic impairment and in patients who have reduced hepatic acetylation status. Adjust dosage based on serum procainamide and NAPA concentrations. **Renal Impairment** Reduction of dosage is required due to accumulation of procainamide and NAPA. Dosage adjustments should be made in conjunction with monitoring of procainamide and NAPA levels, in addition to other factors such as clinical response, patient age, renal status, and hepatic function and acetylator status. Adult patients: Initial dosage adjustment recommendations are as follows: CrCl > 60 mL/min: No initial dosage adjustment is required. CrCl 35 to 59 mL/min: Decrease initial maintenance dosage by approximately 30%. CrCl 15 to 34 mL/min: Decrease initial maintenance dosage by 40% to 60%. CrCl < 15 mL/min: Individualize dosage. Pediatric patients: No specific guidelines are available for pediatric patients with renal impairment; use lower initial doses and adjust as required. Dosage adjustments should be made in conjunction with monitoring of procainamide and NAPA levels, in addition to other factors such as clinical response, patient age, renal status, and hepatic function and acetylator status.

Intermittent hemodialysis
Procainamide and NAPA are removed from the circulation by hemodialysis. Adjust dose based on procainamide and NAPA concentrations.

Peritoneal dialysis
Procainamide and NAPA are not removed from the circulation by peritoneal dialysis.

Pregnancy Cat. Procainamide is classified as FDA pregnancy risk category C

Side Effects:

Severe	Moderate
agranulocytosis pancytopenia aplastic anemia hemolytic anemia hepatic failure arrhythmia exacerbation ventricular tachycardia ventricular fibrillation heart failure asystole torsade de pointes angioedema lupus-like symptoms pericarditis	thrombocytopenia leukopenia neutropenia depression hallucinations psychosis QT prolongation PR prolongation hypotension hyperbilirubinemia elevated hepatic enzymes

Administration:

Intravenous injection:
Each 100 mg of procainamide must be diluted in 10 ml of sterile water for injection or D5W injection.
Inject by slow IV push at a rate not to exceed 50 mg/minute.
Intravenous infusion:
NOTE: According to the manufacturer, procainamide injection is compatible in D5W. However, data indicate procainamide may quickly form an association complex with dextrose. The clinical implications of this complexation are unknown. Refrigeration and pH adjustment may reduce the rate of complexation. Other sources indicate procainamide also is not compatible with D5NS but is compatible with NS and 0.45% NS.
Dilute 0.2—1 gram in 50—500 ml of D5W injection to give an infusion solution containing 2—4 mg/ml. A slight yellow color may be present but it does not alter potency. Discard any solution that has a color darker than light amber or contains a precipitate.
Blood pressure and ECG should be monitored continuously. Prior to administration, the patient should be in the supine position. Using an infusion pump, the initial loading infusion

should be over 30—60 minutes at a rate not to exceed 25—50 mg/minute. Dosage should be adjusted according to patient response, renal function, serum procainamide concentration and, when indicated, serum NAPA concentration.

Other Injectable Administration

Intraosseous infusion

Procainamide is not approved by the FDA for intraosseous administration.

During cardiopulmonary resuscitation in pediatric patients, the same dosage may be given via the intraosseous route when IV access is not available

Adult

For the treatment of ventricular tachycardia with pulses

ACLS recommendation is 20—50 mg/min IV until either the arrhythmia is suppressed, hypotension occurs, the QRS complex is widened by 50%, or the maximum dose of 17 mg/kg is given (Class IIa, Evidence Level B recommendation). Avoid use in patients with prolonged QT and congestive heart failure. Alternatively, 100 mg IV may be administered every 5 minutes until the arrhythmia is suppressed, hypotension occurs, the QRS complex is widened by 50%, or a total of 500 mg has been administered. Then wait at least 10 minutes to allow for distribution to tissues before resuming treatment. If indicated, follow with 1—4 mg/min as a continuous IV infusion. Further dosage should be adjusted according to patient response, renal function, serum procainamide concentration and, when indicated, serum NAPA concentration.

For the treatment of documented ventricular arrhythmias such as sustained ventricular tachycardia in situations other than cardiac arrest; or for the conversion to and/or maintenance of sinus rhythm in patients with paroxysmal atrial tachycardia†, atrial fibrillation† or atrial flutter†; or for the treatment of paroxysmal supraventricular tachycardia (PSVT)†; or for paroxysmal supraventricular tachycardia (PSVT) prophylaxis† in patients with reentrant tachycardia, including patients with Wolff-Parkinson-White (WPW) syndrome†.

Intravenous loading dosage

15—17 mg/kg as an IV infusion, infused at a rate of 20—30 mg/min. Alternatively, 100 mg IV every 5 minutes given by slow IV push until arrhythmia disappears, or up to 1000 mg.

Intravenous maintenance dosage

Initially, 1—4 mg/minute as a continuous IV infusion. The usual initial maintenance dose is about 50 mg/kg/day; lower doses should be used in patients with renal dysfunction or reduced cardiac output. Adjust dosage based on renal function, clinical goals, and serum drug level monitoring.

Pediatric

For the treatment of ventricular tachycardia with pulses

PALS recommendation is 15 mg/kg IV (or intraosseous) over 30—60 minutes.

For the treatment of documented ventricular arrhythmias such as sustained ventricular tachycardia in situations other than cardiac arrest; or for the conversion to and/or maintenance of sinus rhythm in patients with paroxysmal atrial tachycardia†, atrial fibrillation† or atrial flutter†; or for the treatment of paroxysmal supraventricular tachycardia (PSVT)†; or for paroxysmal supraventricular tachycardia (PSVT) prophylaxis† in patients with reentrant tachycardia, including patients with Wolff-Parkinson-White (WPW) syndrome†.

Intravenous loading dosage

3—6 mg/kg IV over 5 minutes. Do not to exceed 100 mg as a single dose. May repeat every 5—10 minutes if needed to a maximum total loading dose of 15 mg/kg. Infusion rate should not exceed 500 mg in 30 minutes.

Intravenous maintenance dosage

The usual dosage is 20—80 mcg/kg/min IV. Maximum dose is 2 g per 24 hours. Adjust dosage based on renal function, clinical goals, and serum drug level monitoring.

Supply: Procainamide/Procainamide Hydrochloride Intramuscular Inj Sol: 1mL, 100mg, 500mg
Procainamide/Procainamide Hydrochloride Intravenous Inj Sol: 1mL, 100mg, 500mg

Notes:

BOXED WARNING

Alcoholism, arrhythmia exacerbation, AV block, bradycardia, bundle-branch block, cardiac arrhythmias, cardiac disease, cardiomyopathy, coronary artery disease, diabetes mellitus, digitalis toxicity, females, heart failure, hypertension, hypocalcemia, hypokalemia, hypomagnesemia, malnutrition, myocardial infarction, QT prolongation, thyroid disease, torsade de pointes, ventricular dysfunction

Procainamide is contraindicated in patients with second- or third-degree AV block unless controlled by a pacemaker due to the risk of additive cardiac depression. In general, use procainamide cautiously in patients with certain types of cardiac disease. Procainamide has proarrhythmic properties and can induce or worsen cardiac arrhythmias. Procainamide should not be used in patients with preexisting heart block, such as first-degree AV block, bundle-branch block, or severe digitalis toxicity, because it can worsen the conduction defect or cause ventricular asystole or fibrillation. Antiarrhythmic agents with proarrhythmic properties (arrhythmia exacerbation), including procainamide and other Class I agents, should not be used in patients with asymptomatic non-life threatening ventricular arrhythmias, especially in patients at risk for proarrhythmic effects such as heart failure, myocardial infarction, or cardiomegaly. Procainamide has not been shown to reduce mortality in patients with non-life-threatening ventricular arrhythmias. There is, however, evidence of an increased risk of death and non-fatal cardiac arrest with the use of flecainide after myocardial infarction in patients with asymptomatic PVCs or non-sustained ventricular tachycardia. Considering the known proarrhythmic properties of procainamide and the lack of evidence of improved survival for antiarrhythmic drugs in patients without life-threatening arrhythmias, the use of procainamide should be reserved for patients with life-threatening ventricular arrhythmias. Procainamide should also be used with caution in patients with congestive heart failure, coronary

artery disease, left ventricular dysfunction, myocardial infarction, acute ischemic heart disease, or cardiomyopathy, since even slight depression of myocardial contractility may further reduce the cardiac output of the damaged heart. In addition, patients with congestive heart failure can have undiagnosed heart block, and the administration of procainamide to such patients would be hazardous. The use of procainamide is contraindicated in patients with torsade de pointes as procainamide can actually aggravate this arrhythmia instead of suppressing it. Similarly, procainamide should be avoided when possible in patients with QT prolongation due to the increased risk of proarrhythmic effects. Use procainamide with caution in patients with cardiac disease or other conditions that may increase the risk of QT prolongation including cardiac arrhythmias, congenital long QT syndrome, heart failure, bradycardia, myocardial infarction, hypertension, coronary artery disease, hypomagnesemia, hypokalemia, hypocalcemia, or in patients receiving medications known to prolong the QT interval or cause electrolyte imbalances. Females, elderly patients, patients with diabetes mellitus, thyroid disease, malnutrition, alcoholism, or hepatic impairment may also be at increased risk for QT prolongation.

- SOME DRUG INTERACTIONS
- **Albuterol; Ipratropium:** (Minor) Beta-agonists should be used cautiously with procainamide. Procainamide administration is associated with QT prolongation and torsades de pointes (TdP). Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses and/or when associated with hypokalemia. Beta-agonists should be administered with extreme caution to patients being treated with drugs known to prolong the QT interval because the action of beta-agonists on the cardiovascular system may be potentiated.
- **Amiodarone:** (Major) Amiodarone may increase procainamide serum concentrations, with potential for drug toxicity. Procainamide and N-acetylprocainamide or NAPA (a pharmacologically active metabolite) serum concentrations increase by approximately 55 and 33%, respectively, during the first 7 days of concomitant amiodarone therapy. The precise pharmacokinetic mechanism of this interaction has not been elucidated, although a reduction the renal clearance of both parent and metabolite, as well as a reduction in hepatic metabolism seem likely. Additive electrophysiologic activity occurs with combination therapy and prolonged QT and QRS intervals or acceleration of preexisting ventricular tachycardia may result. Careful clinical observation of the patient as well as close monitoring of the ECG and serum procainamide and NAPA concentrations is essential with adjustment of the procainamide dosing regimen performed as necessary to avoid enhanced toxicity or pharmacodynamic effects. If amiodarone is to be coadministered with procainamide, the manufacturer recommends reducing the procainamide dosage by 33%. Combination antiarrhythmic therapy is reserved for patients with refractory life-threatening arrhythmias. Due to the extremely long half-life of amiodarone, a drug interaction is possible for days to weeks after discontinuation of amiodarone.
- **Angiotensin II receptor antagonists:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
  Angiotensin-converting enzyme inhibitors: (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
  Anticholinergics: (Moderate) The anticholinergic effects of procainamide may be significant and may be enhanced when combined with anticholinergics.

Anticholinergic agents administered concurrently with procainamide may produce additive antivagal effects on AV nodal conduction, although this is not as well documented for procainamide as for quinidine.

- **Atenolol:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like atenolol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension.
- **Atropine; Edrophonium:** (Moderate) Procainamide has anticholinergic properties and may interfere with the cholinomimetic activity of edrophonium.
- **Azithromycin:** (Major) Due to an increased risk for QT prolongation and torsade de pointes (TdP), caution is advised when administering procainamide with azithromycin. Procainamide is associated with a well-established risk of QT prolongation and TdP, and cases of QT prolongation and TdP have been reported with the post-marketing use of azithromycin.
- **Calcium-channel blockers:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Cimetidine:** (Moderate) H2-blockers, such as cimetidine, inhibit the renal tubular secretion of procainamide. Clearance of procainamide is reduced and serum concentrations are increased by cimetidine.
- **Clarithromycin:** (Major) Clarithromycin should be used cautiously with procainamide. Procainamide and clarithromycin are both associated with a well-established risk of QT prolongation and torsades de pointes (TdP).
- **Diltiazem:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Doxazosin:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Enalapril; Felodipine:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Erythromycin:** (Major) Erythromycin administration is associated with QT prolongation and torsades de pointes (TdP). In addition to potential pharmacokinetic interactions, erythromycin may cause QT prolongation and exhibit additive electrophysiologic effects with procainamide. Concurrent use of erythromycin with procainamide should be avoided.
- **Esmolol:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like esmolol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension.
- **Ethanol:** (Moderate) Alcohol consumption tends to decrease the half-life of procainamide in the blood through induction of its acetylation to NAPA.
- **Fluconazole:** (Major) Procainamide should be used cautiously with fluconazole. Procainamide is associated with a well-established risk of QT prolongation and torsades de pointes (TdP). Fluconazole has been associated with QT prolongation and rare cases of TdP.
- **Haloperidol:** (Major) Haloperidol should be used cautiously with procainamide. Procainamide administration is associated with QT prolongation and torsades de

pointes (TdP). QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation.

- **Labetalol:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like labetalol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension.
- **Levofloxacin:** (Major) Levofloxacin should be avoided in combination with Class IA antiarrhythmics (disopyramide, procainamide, and quinidine). Class IA antiarrhythmics are associated with QT prolongation and torsades de pointes (TdP). Levofloxacin has been associated with prolongation of the QT interval and infrequent cases of arrhythmia. Rare cases of TdP have been spontaneously reported during postmarketing surveillance in patients receiving levofloxacin. According to the manufacturer, levofloxacin should be avoided in patients taking drugs that can result in prolongation of the QT interval.
- **Lidocaine:** (Major) Concurrent use of systemic lidocaine and other antiarrhythmic drugs such as procainamide may result in additive or antagonistic cardiac effects and additive toxicity. Patients receiving more than one antiarrhythmic drug must be carefully monitored; dosage reduction may be necessary.
- **Loop diuretics:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Meperidine:** (Major) Promethazine carries a possible risk of QT prolongation. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with promethazine include procainamide.
- **Methadone:** (Major) The need to coadminister methadone with procainamide should be done with extreme caution and a careful assessment of treatment risks versus benefits. Procainamide administration is associated with QT prolongation and torsades de pointes (TdP). Methadone is considered to be associated with an increased risk for QT prolongation and torsades de pointes (TdP), especially at higher doses (> 200 mg/day but averaging approximately 400 mg/day in adult patients). Laboratory studies, both in vivo and in vitro, have demonstrated that methadone inhibits cardiac potassium channels and prolongs the QT interval. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.
- **Metoprolol:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like metoprolol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension. Procainamide's elimination half-life was not significantly changed when administered concomitantly with metoprolol
- **Nicardipine:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Nitroglycerin:** (Moderate) Nitroglycerin can cause hypotension. This action may be additive with other agents that can cause hypotension such as procainamide.

- **Ofloxacin:** (Major) Class IA antiarrhythmics (such as disopyramide, quinidine, and procainamide) should be used cautiously and with close monitoring with ofloxacin. Class IA antiarrhythmics (such as disopyramide, quinidine, and procainamide) are associated with QT prolongation and torsades de pointes (TdP). Some quinolones, including ofloxacin, have been associated with QT prolongation and infrequent cases of arrhythmia. Post-marketing surveillance for ofloxacin has identified very rare cases of torsades de pointes (TdP).
- **Ondansetron:** (Major) Ondansetron should be used cautiously and with close monitoring with procainamide. If ondansetron and procainamide must be coadministered, ECG monitoring is recommended. Procainamide administration is associated with QT prolongation and torsades de pointes (TdP). Ondansetron has been associated with QT prolongation and post-marketing reports of torsade de pointes (TdP). Among 42 patients receiving a 4 mg bolus dose of intravenous ondansetron for the treatment of postoperative nausea and vomiting, the mean maximal QTc interval prolongation was 20 +/- 13 msec at the third minute after antiemetic administration ($p < 0.0001$).
- **Phenylephrine:** (Major) Promethazine carries a possible risk of QT prolongation. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with promethazine include procainamide.
- **Promethazine:** (Major) Promethazine carries a possible risk of QT prolongation. Drugs with a possible risk for QT prolongation and TdP that should be used cautiously and with close monitoring with promethazine include procainamide.
- **Propranolol:** (Major) High or toxic concentrations of procainamide may prolong AV nodal conduction time or induce AV block; these effects could be additive with the pharmacologic actions of beta-blockers, like propranolol. In general, patients receiving combined therapy with procainamide and beta-blockers should be monitored for potential bradycardia, AV block, and/or hypotension. Procainamide's elimination half-life was not significantly changed when administered concomitantly with propranolol.
- **Ranitidine:** (Moderate) When ranitidine is used in doses more than 300 mg/day, such as those used in the treatment of Zollinger-Ellison syndrome, the renal tubular secretion of procainamide is inhibited; procainamide clearance is reduced leading to elevated procainamide and N-acetyl-procainamide plasma concentrations. It may be prudent to monitor patients for procainamide toxicity if procainamide and high doses of ranitidine are coadministered.
- **Sotalol:** (Major) Sotalol administration is associated with a well-established risk of QT prolongation and torsades de pointes (TdP). Drugs that prolong the QT interval should be used with extreme caution in combination with sotalol. Ventricular tachycardia, including torsade de pointes and monomorphic ventricular tachycardia can occur with excessive prolongation of the QT interval. Examples of agents that may prolong the QT interval include: Class IA antiarrhythmics (disopyramide, procainamide, quinidine). Before initiating sotalol, the previous Class I antiarrhythmic therapy should be withdrawn under careful monitoring for a minimum of (2-3) plasma half-lives for the discontinued drug.
- **Spironolactone:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Tamoxifen:** (Major) Caution is advised with the concomitant use of tamoxifen and procainamide due to an increased risk of QT prolongation and torsade de pointes (TdP). Tamoxifen has been reported to prolong the QT interval, usually in overdose or when used in high doses. Rare case reports of QT prolongation

have also been described when tamoxifen is used at lower doses. Procainamide is associated with a well-established risk of QT prolongation and TdP.

- **Terazosin:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.
- **Terbutaline:** (Minor) Beta-agonists should be used cautiously with procainamide. Procainamide administration is associated with QT prolongation and torsades de pointes (TdP). Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses and/or when associated with hypokalemia. Beta-agonists should be administered with extreme caution to patients being treated with drugs known to prolong the QT interval because the action of beta-agonists on the cardiovascular system may be potentiated.
- **Verapamil:** (Moderate) Procainamide can decrease blood pressure and should be used cautiously in patients receiving antihypertensive agents. Intravenous administration of procainamide is more likely to cause hypotensive effects.

Racepinephrine (Racemic Epinephrine®)

Scope | | **CCT**

Generic Name:	**Racepinephrine**
Trade Name:	Racemic Epinephrine, anthmanefrin, S2 inhalant
Chemical Class:	Alpha/Beta Agonists
Therapeutic Class:	Adrenergic bronchodilator
Actions:	Elicits agonistic action on alpha, beta-2, and beta-2 receptors resulting in bronchial smooth muscle relaxation, cardiac stimulation, vasodilation in skeletal muscle, and stimulation of glycogenolysis in the liver
Pharmacokinetics:	Onset 1-5 minutes. Peak ?. Duration1-3 hours. $t_{½}$ = ?.
Indications:	• Croup
Contraindications:	• Epiglottitis, Long QT syndrome, co-administration with drugs that prolong the QTc (see notes below). Use of MAI inhibitor in the last 14 days (isocarboxazid, linezolid, methylene blue injection, phenelzine, rasagiline, selegiline, tranylcypromine are a few examples).
Precautions:	• Racemic Epi prolongs the QTc so avoid administering with any other drug that increases the QTc. Caution with heart disease, HTN, thyroid disease, diabetes, or urinary retention caused by prostate enlargement.
Pregnancy Cat.	• C
Side Effects:	Tachycardia, Arrhythmias, Headache, Nausea, Sweating, Tremor, Restlessness, Rebound airway edema may occur, Angina Autonomic hyperreflexia, Cardiac dysrhythmia, Ventricular fibrillation Cerebral hemorrhage, Pulmonary edema
Administration:	Inhalation only
Pediatric Croup	< 4 yrs old: 0.05 mL/kg of 2.25% (diluted in at 3 mL of NS) over 15 min. (do not exceed 0.5 mL/dose) > 4yrs old: 0.5 mL of 2.25% solution (diluted in 3 mL of NS) over 15 min.

Supply:	• 11.25mg/0.5mL (2.25% as 1.125% dextro-epinephrine and 1.125% levo-epinephrine)
Notes:	**Some drugs that severely prolong the QTc listed as contrainidcated:** procainamide, quinidine, sotalol, terfenadine. **Some drugs that also prolong the QTc and are listed as "**Serious - Use Alternative": Etomidate, propofol & ketamine increase levels of racemic epinephrine by an unknown mechanism. Amiodarone, amitriptyline, clarithromycin, doxepin, erythromycin, fluconazole, haloperidol, octreotide, promethazine prolong QTc. Propranolol increases effects of racemic epinephrine by pharmacodynamics synergism. Avoid or use alternate drug. Risk of hypertension and bradycardia. Consider selective beta 1 blocker (e.g, metoprolol). **The following drugs are listed as "monitor closely":** Racemic epinephrine and the following drugs all decrease serum potassium: Albuterol, atenolol, gentamicin, isoproterenol, ketololac, norepinephrine, terbutaline, **Some drugs that still prolong the QTc but listed as "monitor closely":** Azithromycin, levofloxacin, ofloxacin.

Ranitidine (Zantac®)

Scope | **CCT**

Generic Name:	**Ranitidine**
Trade Name:	Zantac
Chemical Class:	H2 receptor-agonist
Therapeutic Class:	
Actions:	competitively inhibits the binding of histamine to receptors on gastric parietal cells (designated as the H2-receptor), thus reducing basal and nocturnal gastric acid secretion
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ =2-3 hours.
Indications:	• gastrointestinal disorders such as peptic ulcer and gastroesophageal reflux disease (More potent histamine antagonist than cimetidine).
Contraindications:	• Hypersensitivity to drug, class or component.

	•
Precautions:	• CrCl < 50 ml/min: Reduce recommended dose by 50%. **Porphyria** Rare reports have suggested that ranitidine may precipitate acute porphyric attacks in patients with acute porphyria. It is recommended that ranitidine be avoided in these patients. **Hepatic disease** Because ranitidine is metabolized in the liver, caution should be observed in patients with hepatic disease.
Pregnancy Cat.	B
Side Effects:	pancreatitis hemolytic anemia aplastic anemia agranulocytosis pancytopenia anaphylactoid reactions angioedema interstitial nephritis toxic epidermal necrolysis erythema multiforme bronchospasm vasculitis bradycardia AV block atrophic gastritis sinus tachycardia thrombocytopenia leukopenia hallucinations confusion blurred vision
Administration:	Compatible solutions for dilution include D5W, D10W, NS, lactated ringers. **Intermittent IV infusion** Dilute to a maximum of 0.5 mg/ml using D5W, NS, or other compatible IV solution. Infuse over 15—20 minutes (5—7 ml/minute). Pre-mixed ready-to-use infusion bags are available as 1 mg/ml ranitidine (i.e., 50 mg/50 ml). Premixed ready-to-use bags are for slow IV administration only; infuse over 15—20 minutes. *Adult* 50 mg IV (intermittent infusion) every 6 to 8 hours. *Pediatric*
Supply:	Ranitidine Hydrochloride/Zantac Intravenous Inj Sol: 1mL, 25mg

Notes:

- Ranitidine may impair the release of vasopressin
- **Bradycardia, cardiac disease**

Rarely, bradycardia has been reported with the rapid intravenous administration of ranitidine injection. In most cases, bradycardia was observed in patients with factors predisposing to cardiac rhythm disturbances. When administering ranitidine injection, the recommended rates of administration should not be exceeded; caution is warranted in elderly patients as well as patients with underlining cardiac disease.

Rocuronium®

Scope | | **CCT**

Generic Name:	**Rocuronium**
Trade Name:	Zemuron
Chemical Class:	Non-depolarizing neuromuscular blockade
Therapeutic Class:	Muscle Relaxants, Peripherally Acting
Actions:	Prevents acetylcholine from binding to receptors on the motor end plate, thus blocking action potential transmission, and muscle contraction
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ =.
Indications:	• Rapid sequence intubation or pharmacologically assisted intubation.
Contraindications:	• No absolute contraindications. (Relative contraindication- unable to ventilate patient.)
Precautions: ***Pregnancy Cat.***	•
Side Effects:	Apnea, respiratory insufficiency, bronchospasm, anaphylactoid reactions, angioedema, muscle paralysis, **malignant hyperthermia**, pulmonary hypertension, thorombosis, hiccups, tachycardia, abnormal ECG, transient hypotension, edema, nausea, vomiting.
Administration:	*Adult* **0.6mg/kg to 1.2 mg/kg Maintenance dose to maintain paralysis: 0.1-0.2 mg/kg** *Pediatric*
Supply:	Rocuronium/Rocuronium Bromide/Zemuron Intravenous Inj Sol: 1 mL, 10 mg
Notes:	• May be diluted in NS, D5W, D5NS, sterile water for injection, or lactated Ringer's.

Solu-Cortef®(Hydrocortisone)

Scope CCT

Generic Name:	**Hyrdocortisone**
Trade Name:	A-Hydrocort
Chemical Class:	Cortisol
Therapeutic Class:	Glucocorticoid
Actions:	
Pharmacokinetics:	Onset almost immediate. Peak 1 hr. Duration unknown. $t_{½}$ = 1.5-2 hr (plasma), 1.25-1.5 days for adrenal suppression.
Indications:	• **For the treatment of primary adrenocortical insufficiency (e.g., Addison's disease, congenital adrenal hyperplasia or CAH) or secondary adrenocortical insufficiency.** • **allergic disorders including anaphylaxis, anaphylactic shock, or anaphylactoid reactions, angioedema, acute noninfectious laryngeal edema, drug hypersensitivity reactions, transfusion-related reactions.** • **Septic shock** • **Status asthmaticus**
Contraindications:	• Systemic fungal infections, traumatic brain injury, maleria
Precautions:	**Myocardial infarction** Corticosteroid therapy, such as hydrocortisone, has been associated with left ventricular free-wall rupture in patients with recent myocardial infarction, and should therefore be used cautiously in these patients. **Immunosuppression** Patients receiving high-dose (e.g., equivalent to 1 mg/kg or more of) systemic corticosteroid therapy, such as hydrocortisone, for any period of time, particularly in conjunction with corticosteroid sparing drugs are at risk to develop immunosuppression; patients receiving moderate doses of systemic corticosteroids, such as hydrocortisone, for short periods or low doses for prolonged periods may also be at risk. When given in combination with other immunosuppressive agents, there is a risk of over-immunosuppression.
Pregnancy Cat.	**Teratogenic Effects** Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well-controlled studies in pregnant women. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Side Effects:

Severe

exfoliative dermatitis, increased intracranial pressure, papilledema, tendon rupture, bone fractures ,vascular necrosis, esophageal ulceration, GI perforation, pancreatitis, GI bleeding, peptic ulcer, anaphylactoid reactions, angioedema, heart failure, seizures, optic neuritis, retinopathy, visual impairment ocular hypertension, cardiac arrest, thrombosis, pulmonary edema, stroke, bradycardia, vasculitis, cardiomyopathy, myocardial infarction, arrhythmia exacerbation, thromboembolism.

Administration:

Adult

Treatment of severe conditions such as anaphylaxis, angioedema, acute noninfectious laryngeal edema, or urticarial transfusion-related reactions. Septic shock and/or hypotension in patients whose blood pressure is poorly responsive to adequate fluid resuscitation and vasopressor therapy.

The general dosage is 100 IV; repeat doses as ordered by physician.

Pediatric

Treatment of severe conditions such as anaphylaxis, angioedema, acute noninfectious laryngeal edema, or urticarial transfusion-related reactions. Septic shock and/or hypotension in patients whose blood pressure is poorly responsive to adequate fluid resuscitation and vasopressor therapy**.**

Ask Dr Mel Wright

Supply:

A-Hydrocort/Hydrocortisone/Hydrocortisone Sodium Succinate/Solu-Cortef Intramuscular Inj Pwd F/Sol: 100mg, 250mg, 500mg, 1000mg
A-Hydrocort/Hydrocortisone/Hydrocortisone Sodium Succinate/Solu-Cortef Intravenous Inj Pwd F/Sol: 100mg, 250mg, 500mg, 1000mg

Notes:

- Administer as a 5-10 minute bolus; rapid injection is associated with a high incidence of perianal discomfort.

Terbutaline (Brethine®)

Scope CCT

Generic Name:	**Terbutaline**
Trade Name:	**Brethine®**
Chemical Class:	Adrenergics
Therapeutic Class:	Bronchodilators
Actions:	• Results in the accumulation of cyclic adenosine monophosphate (cAMP) at beta-adrenergic receptors. • Produces bronchodilation. • Inhibits the release of mediators of immediate hypersensitivity reactions from mast cells. • Relatively selective for $beta_2$ (pulmonary)-adrenergic receptor sites, with less effect on $beta_1$ (cardiac)-adrenergic receptors. **Therapeutic Effect(s):** Bronchodilation.
Pharmacokinetics:	**Absorption:** 35–50% absorbed following oral administration but rapidly undergoes first-pass metabolism. Well absorbed following subcut administration. **Distribution:** Enters breast milk. **Metabolism and Excretion:** Partially metabolized by the liver; 60% excreted unchanged by the kidneys following subcut administration. **Half-life:** Unknown. **TIME/ACTION PROFILE (bronchodilation)**

ROUTE	ONSET	PEAK	DURATION
Subcut	within 15 min	within 0.5–1 hr	1.5–4 hr

Indications:	Management of reversible airway disease due to asthma or COPD; inhalation and subcut used for short-term control and oral agent as long-term control. **Unlabeled Use(s):** Management of preterm labor (tocolytic) (the FDA has recommended that injectable terbutaline should not be used in pregnancy for the prevention or prolonged treatment [>48–72 hr] of preterm labor in either the inpatient or outpatient settings because of the potential for serious maternal heart problems and death; oral terbutaline should not be used for the prevention or any treatment of preterm labor because of a lack of efficacy and the potential for serious material heart problems and death).
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity to adrenergic amines. **Use Cautiously in:** • Cardiac disease; • Hypertension; • Hyperthyroidism; • Diabetes;

- Glaucoma;
- Geri: More susceptible to adverse reactions; may require dose ↓
- Excessive use may lead to tolerance and paradoxical bronchospasm (inhaler);
- OB: Lactation: Pregnancy (near term) and lactation.
-

Precautions:

- **Hepatic Impairment**
  No guidelines for dosage adjustment in patients with hepatic impairment are available**.**
- **Renal Impairment**
  CrCl > 50 ml/min: No dosage adjustment is needed.
  CrCl 10—50 ml/min: Give 50% of the usual systemic dose given at the normal dosage interval.
  CrCl < 10 ml/min: Avoid use

Pregnancy Cat: **Terbutaline** is classified as FDA pregnancy risk category B

Side Effects:

CNS: *nervousness*, *restlessness*, *tremor*, headache, insomnia
Resp: pulmonary edema
CV: angina, arrhythmias, hypertension, myocardial ischemia, tachycardia
GI: nausea, vomiting
Endo: hyperglycemia
F and E: hypokalemia
* CAPITALS indicate life-threatening.
Italics indicate most frequent.

Administration:

SC: (Adults and Children ≥12 yr): *Bronchodilation*– 250 mcg; may repeat in 15–30 min (not to exceed 500 mcg/4 hr).

SC: (Children <12 yr): *Bronchodilation*– 0.005–0.01 mg/kg; may repeat in 15–20 min.

IV: (Adults) *Tocolysis*– 2.5–10 mcg/min infusion; ↑ by 5 mcg/min q 10 min until contractions stop (not to exceed 30 mcg/min). After contractions have stopped for 30 min, ↓ infusion rate to lowest effective amount and maintain for 4–8 hr (unlabeled).

Supply: **Injection:** 1 mg/mL

Notes: BOXED WARNING

Premature labor

Terbutaline has been used systemically off-label to reduce contractions of preterm labor and uterine hyperstimulation. Although, certain acute situations may warrant the use of injectable terbutaline in premature labor, its use is not without risk and a boxed warning addresses the use of terbutaline as tocolysis. Oral terbutaline is contraindicated for acute or maintenance tocolysis as its safety and efficacy have not been established. Terbutaline injection has not been approved and should not be used for prolonged tocolysis (beyond 48 to 72 hours). Do not use for maintenance tocolysis in the outpatient or home setting. Serious adverse reactions, including death, have been reported after administration of terbutaline sulfate to pregnant women. In the mother, these adverse reactions include increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema and myocardial ischemia. Increased fetal heart rate and neonatal hypoglycemia may occur as a result of maternal administration. Therefore, terbutaline administered by injection or by continuous infusion pump is contraindicated for prolonged tocolysis (use beyond 48—72 hours).

- Do not confuse Brethine (terbutaline) with Methergine (methylergonovine).
- **SC:** Administer subcut injections in lateral deltoid area. Do not use solution if discolored.
- **IV Administration**
- **Continuous Infusion: Diluent:** May be diluted in D5W, 0.9% NaCl, or 0.45% NaCl. **Concentration:** 1 mg/mL (undiluted).
- **Rate:** Use infusion pump to ensure accurate dose. Begin infusion at 10 mcg/min. Increase dosage by 5 mcg every 10 min until contractions cease. Maximum dose is 80 mcg/min. Begin to taper dose in 5-mcg decrements after a 30–60 min contraction-free period is attained. Switch to oral dose form after patient is contraction-free 4–8 hr on the lowest effective dose.

Torsemide (Demadex®)

Scope | | **CCT**

Generic Name:	**Torsemide**
Trade Name:	Demadex
Chemical Class:	
Therapeutic Class:	Loop Diuretic
Actions:	used for ascites, edema, HTN, and CHF; twice as potent as furosemide allowing a 24-hour dosage interval; may lack the paradoxical antidiuresis seen with furosemide.
Pharmacokinetics:	Onset. Peak. Duration. $t_{½}$ =.
Indications:	• HTN, CHF, Ascites
Contraindications:	• Anuria, hypovolemia, & Hypersensitivity to torsemide
Precautions:	• Excessive diuresis with torsemide should be avoided in patients with acute myocardial infarction due to the risk of precipitating shock.

- Loop diuretics can result in dehydration or hypovolemia, or electrolyte imbalance such as hyponatremia, hypokalemia, hypochloremia, and hypomagnesemia
- Hepatic Disease
- Renal disease

Pregnancy Cat.

B

Side Effects:

Stevens-Johnson syndrome
toxic epidermal necrolysis
angioedema
atrial fibrillation
ventricular tachycardia
thrombosis
oliguria
azotemia
hearing loss
GI bleeding
pancreatitis
hyperglycemia
leukopenia
thrombocytopenia

Administration:

No dilution necessary if given as a slow IV injection.
Administer slowly over a period of 2 minutes.

Adult

HTN	**10 mg IV once daily**
CHF	**20 mg IV once daily**
ascites	**40 mg IV once daily**

Pediatric

Supply:

Notes:

- Based on clinical data of diuretic potency, 10—20 mg IV of torsemide is approximately equivalent to 40 mg IV of furosemide.

Vecuronium (Norcuron®)

Scope CCT

Generic Name:	**Vecuronium**
Trade Name:	**Norcuron®**
Chemical Class:	Paralytic
Therapeutic Class:	Neuromuscular blocking agents-nondepolarizing
Actions:	Prevents neuromuscular transmission by blocking the effect of acetylcholine at the myoneural junction. Has no analgesic or anxiolytic properties **Therapeutic Effect(s):** Skeletal muscle paralysis
Pharmacokinetics:	**Absorption:** Following IV administration, absorption is essentially complete. **Distribution:** Rapidly distributes in extracellular fluid; minimal penetration of the CNS. **Metabolism and Excretion:** Some metabolism by the liver (20%), with conversion to at least one active metabolite; 35% excreted unchanged by the kidneys **Half-life:** Infants: 65 min; Children: 41 min; Adults: 65–75 min (↓ near term in pregnant patients, ↑ in hepatic impairment). **TIME/ACTION PROFILE**

ROUTE	ONSET	PEAK	DURATION
IV	1–3 min	3–5 min	30–40 min

Indications:	• Induction of skeletal muscle paralysis and facilitation of intubation after induction of anesthesia in surgical procedures. • Facilitation of compliance during mechanical ventilation.
Contraindications/ Considerations:	**Contraindicated in:** • Hypersensitivity • Hypersensitivity to bromides **Use Cautiously in:** • Dehydration or electrolyte abnormalities (should be corrected) • Fractures or muscle spasm • Hyperthermia (↑ duration/intensity of paralysis) • Significant hepatic impairment • Shock • Extensive burns (may be more resistant to effects) • Low plasma pseudocholinesterase levels (may be seen in association with anemia, dehydration, cholinesterase inhibitors/insecticides, severe liver disease, pregnancy, or hereditary predisposition) • Obese patients • OB: Lactation: Safety not established (use only if benefit outweighs potential risk to fetus) • Pedi: Children <7 wk (safety and effectiveness not established) **Exercise Extreme Caution in:**

	Neuromuscular diseases such as myasthenia gravis (small test dose may be used to assess response).
Precautions:	• **Hepatic Impairment** Hepatic impairment may prolong the duration of action of vecuronium. Specific guidelines for dosage adjustments in hepatic impairment are not available; dosage reduction or extended dosing interval may be necessary**.** • **Renal Impairment** Renal failure may prolong the duration of action of vecuronium. Specific guidelines for dosage adjustments in patients with renal impairment and failure are not available; dosage reduction or extended dosing interval may be necessary in patients with renal failure. However, the manufacturer states that if prepared well for surgery with dialysis, patients with renal failure tolerate vecuronium well without a significant prolongation of clinical effect. If anephric patients cannot be prepared for surgery with dialysis, a lower initial dose should be considered.
Pregnancy Cat:	**Vecuronium** is classified as FDA pregnancy risk category C
Side Effects:	**Resp:** bronchospasm **Derm:** rash **Misc:** ALLERGIC REACTIONS INCLUDING ANAPHYLAXIS * CAPITALS indicate life-threatening. *Italics* indicate most frequent.
Administration:	**IV: (Adults and Children >10 yr):** *Intubation*– 0.08–0.1 mg/kg (0.06–0.085 mg/kg if given after steady-state anesthesia achieved or 0.04–0.06 mg/kg after succinylcholine-assisted intubation and anesthesia; wait for disappearance of succinylcholine effects; or 0.05–0.06 mg/kg during balanced anesthesia); *Maintenance dose*– 0.01–0.015 mg/kg 25–40 min after initial dose, then q 12–15 min as needed; *Continuous infusion*– 0.8–1.2 mcg/kg/min. **IV: (Children 1–10 yr):** 0.1 mg/kg q 1 hr as needed. **IV: (Infants 7 wk– 1 yr):** 0.1 mg/kg q 1 hr as needed or as a continuous infusion of 1–1.5 mcg/kg/min.
Supply:	**Powder for injection:** 10 mg/vial, 20 mg/vial
Notes:	• **High Alert Medication:** This medication bears a heightened risk of causing significant patient harm when it is used in error. • **High Alert:** Unplanned administration of a neuromuscular blocking agent instead of administration of the intended medication or administration of a neuromuscular blocking agent in the absence of ventilatory support has resulted in serious harm and death. Confusing similarities in packaging and insufficiently controlled access to these medications are often implicated in these medication errors. • Dose is titrated to patient response. o Vecuronium has *no* effect on consciousness or pain threshold. Adequate anesthesia/analgesia should *always* be used when vecuronium is used as an adjunct to surgical procedures or when

painful procedures are performed. Benzodiazepines and/or analgesics should be administered concurrently when prolonged vecuronium therapy is used for ventilator patients, because patient is awake and able to feel all sensations.
    - If eyes remain open throughout prolonged administration, protect corneas with artificial tears.
- **IV:** Reconstitute with bacteriostatic water (may be provided by manufacturer), D5W, 0.9% NaCl, D5/0.9% NaCl, or LR injection. Solution reconstituted with bacteriostatic water is stable if refrigerated for 5 days. If other diluents are used, solution is stable for 24 hr if refrigerated. Discard all unused solution.
- **IV Push: Concentration:** Maximum of 2 mg/ml. Titrate dose according to patient response.
- **Continuous Infusion: Diluent:** Dilute to a concentration of 1 mg/ml in D5W, 0.9% NaCl, or LR. Use sterile water for injection instead of manufacturer-provided diluent (contains benzyl alcohol) when reconstituting for use in neonates.
- **Rate:** Titrate rate of infusion according to patient response.