HUMAN-LABELED PRODUCTS:

Ephedrine Sulfate Capsules: 25 mg; generic (West-Ward); (OTC)

Ephedrine Sulfate Injection: 50 mg/mL in 1 mL vials & preservative free in 1 mL amps; generic; (Rx)

In the USA, ephedrine sulfate is classified as a list 1 chemical (drugs that can be used as precursors to manufacture methamphetamine) and in some states it may be a controlled substance or have other restrictions placed upon its sale. Be alert to persons desiring to purchase this medication.

EPINEPHRINE

(ep-i-*nef*-rin) Adrenalin®

ALPHA- & BETA-ADRENERGIC AGONIST

Prescriber Highlights

- Alpha- & beta-adrenergic agonist agent used systemically for treating anaphylaxis & cardiac resuscitation
- Contraindications: Narrow-angle glaucoma, hypersensitivity to epinephrine, shock due to non-anaphylactoid causes, during general anesthesia with halogenated hydrocarbons, during labor (may delay the second stage), cardiac dilatation or coronary insufficiency; cases where vasopressor drugs are contraindicated (*e.g.*, thyrotoxicosis, diabetes, hypertension, toxemia of pregnancy)
- Use extreme caution patients with a prefibrillatory cardiac rhythm
- Caution: Hypovolemia (not a substitute for adequate volume replacement)
- Do not inject with local anesthetics into small appendages of the body (*e.g.*, toes, ears, etc.); may cause necrosis/sloughing
- Adverse Effects: Anxiety, tremor, excitability, vomiting, hypertension (overdosage), arrhythmias, hyperuricemia, & lactic acidosis (prolonged use or overdosage)
- Concentrations must not be confused
- Drug interactions

Uses/Indications

Epinephrine is employed primarily in veterinary medicine as a treatment for anaphylaxis or cardiac resuscitation. Because of its vasoconstrictive properties, epinephrine is added to local anesthetics to retard systemic absorption and prolong effect.

Pharmacology/Actions

Epinephrine is an endogenous adrenergic agent that has both alpha and beta activity. It relaxes smooth muscle in the bronchi and the iris, antagonizes the effects of histamine, increases glycogenolysis, and raises blood sugar. If given by rapid IV injection it causes direct stimulation of the heart (increased heart rate and contractility), and increases systolic blood pressure. If given slowly IV, it usually produces a modest rise in systolic pressure and a decrease in diastolic blood pressure. Total peripheral resistance is decreased because of beta effects.

Pharmacokinetics

Epinephrine is well-absorbed following IM or SC administration. IM injections are slightly faster absorbed than SC administration; absorption can be expedited by massaging the injection site. Epinephrine is rapidly metabolized in the GI tract and liver after oral administration and is not effective via this route. Following SC injection, the onset of action is generally within 5–10 minutes. The onset of action following IV administration is immediate and intensified.

Epinephrine does not cross the blood-brain barrier, but does cross the placenta and is distributed into milk.

Epinephrine's actions are ended primarily by the uptake and metabolism of the drug into sympathetic nerve endings. Metabolism takes place in both the liver and other tissues by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT) to inactive metabolites.

Contraindications/Precautions/Warnings

Epinephrine is contraindicated in patients with narrow-angle glaucoma, hypersensitivity to epinephrine, shock due to non-anaphylactoid causes, during general anesthesia with halogenated hydrocarbons or cyclopropane, during labor (may delay the second stage), and cardiac dilatation or coronary insufficiency. Epinephrine should also not be used in cases where vasopressor drugs are contraindicated (*e.g.*, thyrotoxicosis, diabetes, hypertension, toxemia of pregnancy). It should not be injected with local anesthetics into small appendages of the body (*e.g.*, toes, ears, etc.) because of the chance of necrosis and sloughing.

Use epinephrine with caution in cases of hypovolemia; it is not a substitute for adequate fluid replacement therapy. It should be used with extreme caution in patients with a prefibrillatory cardiac rhythm, because of its excitatory effects on the heart. While epinephrine's usefulness in asystole is well documented, it can cause ventricular fibrillation; use cautiously in cases of ventricular fibrillation.

Adverse Effects

Epinephrine can induce feelings of fear or anxiety, tremor, excitability, vomiting, hypertension (overdosage), arrhythmias (especially if patient has organic heart disease or has received another drug that sensitizes the heart to arrhythmias), hyperuricemia, and lactic acidosis (prolonged use or overdosage). Repeated injections can cause necrosis at the injection site.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

It is not known if this drug is excreted in milk.

Overdosage/Acute Toxicity

Clinical signs seen with overdosage or inadvertent IV administration of SC or IM dosages can include: sharp rises in systolic, diastolic, and venous blood pressures, cardiac arrhythmias, pulmonary edema and dyspnea, vomiting, headache, and chest pain. Cerebral hemorrhages may result because of the increased blood pressures. Renal failure, metabolic acidosis and cold skin may also result.

Because epinephrine has a relatively short duration of effect, treatment is mainly supportive. If necessary, the use an alpha-adrenergic blocker (*e.g.*, phentolamine) or a beta-adrenergic blocker (*e.g.*, propranolol) can be considered to treat severe hypertension and cardiac arrhythmias. Prolonged periods of hypotension may follow, which may require treatment with norepinephrine.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving epinephrine and may be of significance in veterinary patients:

- **ALPHA-BLOCKERS** (*e.g.*, **phentolamine**, **phenoxybenzamine**, **prazosin**): May negate the therapeutic effects of epinephrine
- **ANESTHETICS, GENERAL:** An increased risk of arrhythmias developing can occur if epinephrine is administered to patients who have received cyclopropane or a halogenated hydrocarbon anesthetic agent. Propranolol may be administered should these occur.
- **ANTIHISTAMINES:** Certain antihistamines (**diphenhydramine**, **chlorpheniramine**, etc.) may potentiate the effects of epinephrine
- **BETA-BLOCKERS:** Propranolol (or other beta-blockers) may potentiate hypertension, and antagonize epinephrine's cardiac and bronchodilating effects by blocking the beta effects of epinephrine
- **DIGOXIN:** An increased risk of arrhythmias may occur if epinephrine is used concurrently with digitalis glycosides
- **NITRATES:** May reverse the pressor effects of epinephrine
- **LEVOTHYROXINE:** May potentiate the effects of epinephrine
- **OXYTOCIC AGENTS:** Hypertension may result if epinephrine is used with oxytocic agents
- **SYMPATHOMIMETIC AGENTS, OTHER:** Epinephrine should not be administered with other sympathomimetic agents (*e.g.*, **isoproterenol**) as increased toxicity may result
- **PHENOTHIAZINES:** May reverse the pressor effects of epinephrine
- **RESERPINE:** May potentiate the pressor effects of epinephrine
- **TRICYCLIC ANTIDEPRESSANTS:** May potentiate the effects of epinephrine

Doses

Note: Be certain when preparing injection that you do not confuse 1:1000 (1 mg/mL) with 1:10,000 (0.1 mg/mL) concentrations. To convert a 1:1000 solution to a 1:10,000 solution for IV or intratracheal use, dilute each mL with 9 mL of normal saline for injection. Epinephrine is only one aspect of treating cardiac arrest; refer to specialized references or protocols for more information.

- **DOGS:**

  Cardiac resuscitation (asystole):

  a) Both high dose (0.1–0.2 mg/kg) and low dose (0.01–0.02 mg/kg) IV or IO epinephrine have been advocated. In human medicine, generally the low dose is attempted first and if no response go to the high dose. In veterinary medicine (at present), either dose seems acceptable. Doses may be repeated at 3–5 minute intervals if there is no response. (Drobatz 2004)

  b) Although controversial, high dose epinephrine (0.2 mg/kg) is probably more effective than low dose (0.02 mg/kg for cardiopulmonary cerebral resuscitation. It can be given every 3–5 minutes IV, preferably in a central vein. If venous access is not obtained, multiply the dose by 2–10 times and administer into the distal trachea with a syringe and a red rubber tube. (Proulx 2002)

  c) 0.01–0.1 mg/kg IV or IT q2–5 minutes (Rozanski 2002)

  For anaphylaxis:

  a) 0.01–0.02 mg/kg IV; or the dosage may be doubled and given via the endotracheal tube if IV line is not yet established. In less severe cases, may be given IM or SC (Cohen 1995)

  b) 0.2–0.5 mg (total dose) SC or IM (Wohl 2005)

  c) For bronchoconstriction: 20 mcg/kg (0.02 mg/kg) IV, IM, SC, or IT (Johnson 2000)

  For treatment of hypotension associated with anesthesia:

  a) 0.05–0.4 mcg/kg/min IV (Dodam 2005), (Mazzaferro 2005)

- **CATS:**

  For cardiac resuscitation: 0.05–0.5 mg (0.5–5 mL) of 1:10,000 solution intratracheally or intravenously. May need to repeat every 5 minutes. If intratracheal or IV sites are inaccessible, the intracardiac (IC) route may be used. IC dose is 0.5 to 5 micrograms/kg (0.0005 to 0.005 mg/kg). (Wingfield 1985)

  For bronchoconstriction/anaphylaxis:

  a) 0.01–0.02 mg/kg IV; or the dosage may be doubled and given via the endotracheal tube if IV line is not yet established. In less severe cases, may be given IM or SC. (Cohen 1995)

  b) 20 mcg/kg (0.02 mg/kg) IV, IM, SC, or IT (Johnson 2000)

  For feline asthma/anaphylaxis:

  a) 0.1 mL of a 1:1,000 dilution SC or IV (Noone 1986)

  b) Dilute 1 mL of 1:1,000 in 10 mL of saline and give 1 mL/10 kg body weight IV or IM. May repeat q5–15 minutes. (Kittleson 1985a)

- **BIRDS:**

  a) 0.1 mg/kg IV or intracardiac (Harris 2003)

- **HORSES:** (**Note:** ARCI UCGFS Class 2 Drug)

  For anaphylaxis:

  a) 3–5 mL of 1:1,000 per 450 kg of body weight either IM or SC; For foal resuscitation: 0.1 mL/kg of 1:1,000 IV (preferably diluted with saline) (Robinson 1987)

  For cardiopulmonary resuscitation of newborn foals:

  a) 0.01–0.02 mg/kg (0.5–1 mL of a 1:1000 solution for a 50 kg foal) IV every 3 minutes until return of spontaneous circulation. If given intratracheally (IT), dose is 0.1–0.2 mL/kg. (Corley 2003)

- **RUMINANTS, SWINE:**

  For treatment of anaphylaxis:

  a) 0.5–1 mL/100 lbs. body weight of 1:1,000 SC or IM; dilute to 1:10,000 if using IV; may be repeated at 15 minute intervals Often used in conjunction with corticosteroids and diphenhydramine (Clark 1986)

Monitoring

- Cardiac rate/rhythm
- Respiratory rate/auscultation during anaphylaxis
- Urine flow, if possible
- Blood pressure and blood gases, if indicated and possible

Client Information

- Pre-loaded syringes containing an appropriate amount of epinephrine may be dispensed to clients for treatment of anaphylaxis in animals with known hypersensitivity.
- Anaphylactic clinical signs (depending on species) should be discussed.
- Clients should be instructed in proper injection technique (IM or SC) and storage conditions for epinephrine.
- Do not use epinephrine if it is outdated, discolored, or contains a precipitate.

Chemistry/Synonyms
An endogenous catecholamine, epinephrine occurs as white to nearly white, microcrystalline powder or granules. It is only very slightly soluble in water, but it readily forms water-soluble salts (*e.g.*, HCl) when combined with acids. Both the commercial products and endogenous epinephrine are in the Levo form, which is about 15 times more active than the dextro-isomer. The pH's of commercial injections are from 2.5–5.

Epinephrine is commonly called adrenalin.

Storage/Stability/Compatibility
Epinephrine HCl for injection should be stored in tight containers protected from light. Epinephrine will darken (oxidation) upon exposure to light and air. Do not use the injection if it is pink, brown, or contains a precipitate. The stability of the injection is dependent on the form and the preservatives present and may vary from one manufacturer to another. Epinephrine is rapidly destroyed by alkalies, or oxidizing agents.

Epinephrine HCl is reported to be physically **compatible** with the following intravenous solutions and drugs: Dextran 6% in dextrose 5%, Dextran 6% in normal saline, dextrose-Ringer's combinations, dextrose-lactated Ringer's combinations, dextrose-saline combinations, dextrose 2.5%, dextrose 5% (becomes unstable at a pH >5.5), dextrose 10%, Ringer's injection, lactated Ringer's injection, normal saline, and sodium lactate 1/6 M, amikacin sulfate, cimetidine HCl, dobutamine HCl, metaraminol bitartrate, and verapamil HCl.

Epinephrine HCl is reported to be physically **incompatible** with the following intravenous solutions and drugs: Ionosol-D-CM, Ionosol-PSL (Darrow's), Ionosol-T with dextrose 5% (**Note:** other Ionosol product are compatible), sodium chloride 5%, and sodium bicarbonate 5%, aminophylline, cephapirin sodium, hyaluronidase, mephentermine sulfate, sodium bicarbonate, and warfarin sodium. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

Epinephrine HCl for Injection 1 mg/mL (1:1,000) in 1 mL amps and syringes and 10 mL, 30 mL and 100 mL vials; *Amtech® Epinephrine Injection USP* (Phoenix Scientific); *Am-Vet® Epinephrine 1:000* (Neogen); Epinephrine (Vedco, Vet Tek); *Epinject®* (Vetus); *Epinephrine 1:000* (AgriPharm, Durvet, Bimeda, Butler, Phoenix Pharmaceutical); Epinephrine Injection (AgriLabs); (Rx). Labeled for dogs, cats, cattle, horses, sheep and swine.

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Epinephrine HCl for Injection: 1 mg/mL (1:1000) in 1 mL amps, 5 mL vials, 0.3 mL single dose auto-injectors; *Adrenalin Chloride®* (Monarch); *EpiPen®* (Dey); generic; (Abbott); (Rx)

Epinephrine HCl for Injection: 0.5 mg/mL (1:2000) in 0.3 mL single dose auto-injectors; *EpiPen Jr®* (Dey); (Rx)

Epinephrine HCl for Injection: 0.1 mg/mL (1:10,000) in 10 mL syringes & vials; generic, (Abbott); (Rx)

Epinephrine bitartrate is available as a powder form (aerosol) for inhalation, topical solution and a solution for nebulization; ophthalmic preparations are available.

EPOETIN ALFA
ERYTHROPOIETIN

(eh-*poe*-ee-tin *al*-fah) EPO, rHuEPO, Epogen®, Procrit®

ERYTHROPOETIC AGENT

Prescriber Highlights
- Hormone that regulates erythropoiesis; used for anemia associated with chronic renal failure
- Contraindications: Patients with uncontrolled hypertension or in those who are hypersensitive to it
- Adverse Effects: Autoantibodies with resultant resistance to treatment, hypertension, seizures, iron depletion, local reactions at injection sites, fever, arthralgia, & mucocutaneous ulcers
- Adequate monitoring vital

Uses/Indications
EPO has been used to treat dogs and cats for anemia associated with chronic renal failure. Some clinicians state that because of the expense and potential risks associated with its use, PCV's should be in the "teens" before considering beginning EPO therapy. Development of antibodies to EPO has severely limited its clinical usefulness in veterinary medicine for chronic use. EPO may be demonstrated in the future to have significant benefits in reducing the number or volume of transfusions, or as a neuroprotective agent.

Pharmacology/Actions
Erythropoietin is a naturally occurring substance produced in the kidney and considered a hormone as it regulates erythropoiesis. It stimulates erythrocyte production by stimulating the differentiation and proliferation of committed red cell precursors. EPO also stimulates the release of reticulocytes.

Recombinant Human EPO alfa (r-HuEPO-alpha) serves as a substitute for endogenous EPO, primarily in patients with renal disease. Various uremic toxins may be responsible for the decreased production of EPO by the kidney.

Pharmacokinetics
EPO is only absorbed after parenteral administration. It is unclear whether the drug crosses the placenta or enters milk. The drug's metabolic fate is unknown. In patients with chronic renal failure, half-lives are prolonged approximately 20% over those with normal renal function. Depending on initial hematocrit and dose, correction of hematocrit may require 2–8 weeks.

Contraindications/Precautions/Warnings
EPO is contraindicated in patients with uncontrolled hypertension or in those who are hypersensitive to it (see Adverse Effects below). EPO cannot be recommended for use in equines. In animals with moderate to severe hypertension or iron deficiency, therapy should be started with caution or withheld until corrected.

Patients receiving EPO, generally require exogenous administration of iron supplements.

Adverse Effects
In dogs and cats, the most troublesome aspect of EPO therapy is the development of autoantibodies (20–70% incidence) with resultant resistance to further treatment. Perhaps up to 30% of all patients will develop antibodies significant enough to cause profound anemia,