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,

arrestment of erythropoiesis, and transfusion dependency. Should a patient develop refractory anemia while receiving adequate EPO doses and have normal iron metabolism, a bone marrow aspirate should be considered. A myeloid:erythroid ratio of greater than 6 predicts significant autoantibody formation and contraindicates further EPO therapy. Some clinicians believe that the drug (EPO) should be withdrawn if PCV starts to drop while on therapy.

Other effects reported include: systemic hypertension, high blood viscosity, seizures, and iron depletion. Local reactions at injection sites (which may be a predictor of antibody formation), fever, arthralgia, and mucocutaneous ulcers are also possible. Other effects that have been noted that may be a result of the animal's disease (or compounded by such), include cardiac disease (may be related to hypertension associated with chronic renal failure). In humans, hyperkalemia, seizures, and iron deficiency have been reported.

Therapy should be discontinued if any of the following are recognized: polycythemia, fever, anorexia, joint pain, cellulitis, cutaneous or mucosal ulceration (Cowgill 2002).

Reproductive/Nursing Safety

Some teratogenic effects (decrease in body weight gain, delayed ossification, etc.) have been noted in pregnant rats given high dosages. Rabbits receiving 500 mg/kg during days 6–18 of gestation showed no untoward effects on offspring; however, use during pregnancy only when benefits outweigh the potential risks. 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 whether epoetin alfa is excreted in milk, but it is unlikely to pose much risk to nursing offspring.

Overdosage/Acute Toxicity

Acute overdoses appear to be relatively free of adverse effects. Single doses of up to 1600 Units/kg in humans demonstrated no signs of toxicity. Chronic overdoses may lead to polycythemia or other adverse effects. Cautious phlebotomy may be employed should polycythemia occur.

Drug Interactions

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

- **ANDROGENS:** May increase the sensitivity of erythroid progenitors; this interaction has been used for therapeutic effect; (**Note:** This effect has not been confirmed in well-controlled studies nor has the safety of this combination been determined.)
- **DESMOPRESSIN:** With EPO can decrease bleeding times
- **PROBENECID:** Probenecid has been demonstrated to reduce the renal tubular excretion of EPO; clinical significance remains unclear at this time

Laboratory Considerations

No laboratory interactions of major clinical importance have been described.

Doses

- **DOGS:**

  As adjunctive therapy for the treatment of anemia associated with end-stage renal disease:

  a) Initially, 100 Units/kg SC 3 times weekly, until the bottom of the target hematocrit range of 37–45% is attained. Once the lower range of the target hematocrit is attained, the dosing interval is changed to twice weekly. As the hematocrit approaches the upper target value, reduce to once weekly. The dosage schedule is then further modified as required and EPO administered between one and three times weekly to maintain hematocrit within the target range.

  A lower initial dosage of 50–100 Units/kg 3 times weekly may be used if slower response is acceptable and appropriate for the patient. If adequate control is not achieved within 8–12 weeks, then dose can be increased by an additional 25–50 Units/kg every 3–4 weeks while maintaining dosing interval at 3 times a week. Withhold treatment temporarily if hematocrit exceeds target range. Once hematocrit is reestablished at the upper limit of the target range, re-institute treatment at a lower dosing schedule. Do not adjust dosage or dosing interval more often than once every three weeks (due to the long lag time for a response). Generally, a maintenance dose of 75–100 U/kg SC 1–2 times weekly is sufficient (not less than once per week, and not more than 3 times a week). Iron supplementation required. (Cowgill 2002)

  b) Initially, 48.4–145 units/kg SC three times a week. Most dogs and cats should be started at 97 units/kg SC 3 times a week. Use high end dose initially when anemia is severe (HCT less than 14%) and low end dose if hypertension is present or when anemia is not severe. Monitor hematocrit weekly until a target hematocrit of 37–45% is reached. When hematocrit reaches low end of target decrease dosing to two times weekly. Continue monitoring and adjusting dose and frequency as necessary, but take lag phase into account and do not adjust too rapidly. If animal requires >145 units/kg three times a week, evaluate for epoetin resistance. Oral iron supplements recommended for all patients on epoetin. (Polzin, Osborne et al. 2000)

- **CATS:**

  As adjunctive therapy for the treatment of anemia associated with end-stage renal disease:

  a) As above (for each specific author), but the target hematocrit is: 30–40%. (Cowgill 2002), (Polzin, Osborne et al. 2000)

  b) Consider using epoetin when PCV is <20%; dose at 75–100 U/kg SC three times a week until PCV is in the low normal range (35%), then reduce dose and frequency to 50–75 U/kg two times per week. Monitor PCV and blood pressure. It is important to administer iron at start of regime and until appetite is good. (Scherk 2003d)

- **FERRETS:**

  a) 50–150 IU/kg IM 3 times weekly; may decrease to once weekly if RBC indices are significantly improved (Williams 2000)

- **RABBITS/RODENTS/SMALL MAMMALS:**

  a) Rabbits: 50–150 IU/kg SC every 2–3 days until PVC is normal; then once weekly (q7 days) for at least 4 weeks (Ivey and Morrisey 2000)

Monitoring

- Hematocrit; PCV; (Initially weekly to every other week for 2–4 months, then when dose and Hct are stable, at 1–2 month intervals)
- Blood Pressure (initially, at least monthly then every 1–2 months thereafter)
- Renal Function Status
- Iron status (serum iron, TIBC), RBC indices (initially and regularly during therapy to insure adequate iron availability)

Client Information
- For outpatient administration, training in proper injection techniques, drug handling and storage should be performed

Chemistry/Synonyms
A biosynthetic form of the glycoprotein human hormone erythropoietin, epoetin alfa (EPO) has a molecular weight of approximately 30,000. It is commercially available as a sterile, preservative-free, colorless solution. Sodium chloride solution is added to adjust tonicity and is buffered with sodium citrate or citric acid. Human albumin (2.5 mg per vial) is also added to the solution.

Epoetins may also be known by the following synonyms and internationally registered trade names: erythropoietin, r-HuEPO, BI-71.052 (epoetin gamma), BM-06.019 (epoetin beta), EPO (epoetin alfa), EPOCH (epoetin beta), *Bioyetin®*, *Culat®*, *Epogin®*, *Epomax®*, *Epopen®*, *Epotin®*, *Epoxitin®*, *Eprex®*, *Erantin®*, *Eritina®*, *Eritrogen®*, *Eritromax®*, *Erypo®*, *Espo®*, *Exetin-A®*, *Globuren®*, *Hemax®*, *Hemax-Eritron®*, *Hypercri®*, *Mepotin®*, *NeoRecormon®*, *Neorecormon®*, *Procrit®*, *Pronivel®*, *Recormon®*, *Repotin®*, *Tinax®*, and *Wepox®*.

Storage/Stability/Compatibility
The injectable solution should be stored in the refrigerator (2-8°C); do not freeze. Do not shake the solution as denaturation of the protein with resultant loss of activity may occur. If light exposure is limited to 24 hours or less, no effects on potency should occur. When stored as directed, the solution has an expiration date of 2 years after manufacture. Do not mix with other drugs or use the same IV tubing with other drugs running. Because the solution contains no preservatives, the manufacturer recommends using each vial only as a single use.

A method of diluting the Amgen product to facilitate giving very small dosages has been described (Grodsky 1994). Using a 1:20 dilution (1 part *Epogen®* to 19 parts bacteriostatic normal saline does not require any additional albumin to prevent binding of the drug to container). No data is available commenting on this dilution's stability.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. It is also prohibited on the premises of a racing facility.

HUMAN-LABELED PRODUCTS:

Epoetin Alfa, Recombinant for Injection: 2000 units/mL, 3000 units/mL, 4000 units/mL, 10,000 units/mL, 20,000 units/mL and 40,000 units/mL in 1 mL and 2 mL (10,000U only) both single-dose and multidose vials; *Epogen®* (Amgen), *Procrit®* (Ortho Biotech); (Rx)

EPRINOMECTIN

(e-pri-no-***mek***-tin) Ivomec® Eprinex®

TOPICAL AVERMECTIN ANTIPARASITIC AGENT

Prescriber Highlights
- Topically applied avermectin antiparasiticide for cattle
- Used as labeled; there are no milk or meat withdrawal times required

Uses/Indications
In cattle, eprinomectin is indicated for a variety gastrointestinal roundworms including adult and L4 stages of *Haemonchus placei, Ostertagia ostertagi, Trichostrongylus axei* and *colubriformis, Cooperia oncophora/punctata/surnabada, Nematodirus helvetianus, Oesophagostomum radiatum, Bunostomum phlebotomum*, and *Trichuris* spp. (adults only); cattle grubs; lice; mange mites; horn flies (for 7 days after treatment), and lungworms (*Dictyocaulus vivaparus*—for 21 days after treatment).

Topical eprinomectin may be useful for the topical treatment of ear mites (*Psoroptes cuniculi*) in rabbits. One small study (6 subjects) showed partial response when rabbits were dosed at 5 mg/kg topically, twice at 14 day intervals. (Ulutas, Voyvoda et al. 2005)

Pharmacology/Actions
Eprinomectin binds selectively to glutamate-gated chloride ion channels that occur in invertebrate nerve and muscle cells. This leads to an increase in cell membrane permeability to chloride ions, leading to paralysis and death of the parasite. Like ivermectin, eprinomectin enhances the release of gamma amino butyric acid (GABA) at presynaptic neurons. GABA acts as an inhibitory neurotransmitter and blocks the post-synaptic stimulation of the adjacent neuron in nematodes or the muscle fiber in arthropods. These compounds are generally not toxic to mammals as they do not have glutamate-gated chloride channels and do not readily cross the blood-brain barrier.

Pharmacokinetics
No information noted.

Contraindications/Precautions/Warnings
Do not give orally or intravenously.

Adverse Effects
At the time of review, no adverse reactions have been reported.

Overdosage/Acute Toxicity
Calves given up to 5X dosage showed no signs of adverse effects. One subject (of 6) showed signs of mydriasis when given a 10X dose.

Drug Interactions
No interactions noted

Doses
- **CATTLE:**

  For labeled indications:

  a) 1 mL per 10 kg (22 lb) body weight applied topically along backline in a narrow strip from the withers to the tailhead (Package Insert; *Ivomec® Eprinex®*—Merial)

Client Information
- When used as labeled, there are no milk or meat withdrawal times required.
- Weather conditions (including rainfall) during administration do not affect efficacy.
- Do not apply to backline if covered with mud or manure.
- Dispose of containers in an approved landfill or by incineration; do not contaminate water as eprinomectin may adversely affect fish and aquatic organisms.

Chemistry/Synonyms
A member of the avermectin-class of antiparasitic agents, eprinomectin is also known as MK-397 or 4-epi-acetylamino-4-deoxy-avermectin B1.