Chemistry/Synonyms

A fluoroquinolone antibiotic, enrofloxacin occurs as a pale yellow, crystalline powder. It is slightly soluble in water. Enrofloxacin is related structurally to the human-approved drug ciprofloxacin (enrofloxacin has an additional ethyl group on the piperazinyl ring)

Enrofloxacin may also be known as: Bay-Vp-2674 or *Baytril®*.

Storage/Stability/Compatibility

Unless otherwise directed by the manufacturer, enrofloxacin tablets should be stored in tight containers at temperatures less than 30°C. Protect from strong UV light. Enrofloxacin has been reported to be soluble and stable in water, but solubility is pH dependent and altering the pH of the commercially available injections can cause precipitation.

The canine-approved product (2.27%) for IM injection should be stored protected from light; do not freeze.

The cattle-approved product (10%) injectable solution should be stored protected from sunlight. It should not be refrigerated, frozen or stored above 40°C (104°F). If exposed to cold temperatures, precipitation may occur; to redissolve, warm and then shake the vial.

Injectable enrofloxacin must not be mixed with, or come into contact with any IV solution containing magnesium (*e.g.*, *Normosol-R*, *Plasmalyte-R, -A,* or *-56*); morbidity and mortality secondary to micro-precipitants lodging in patient lungs have been reported.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Enrofloxacin Tablets (Film-Coated) & Oral Taste Tablets: 22.7 mg, 68 mg, 136 mg; *Baytril®* (Bayer Corp); (Rx). Approved for use in dogs and cats.

Enrofloxacin Injection: 22.7 mg/mL (2.27%) in 20 mL vials; *Baytril®* (Bayer Corp); (Rx). Approved for use in dogs.

Enrofloxacin Injection: 100 mg/mL in 100 mL and 250 mL bottles. Approved for use in cattle only. Not for use in cattle intended for dairy production or in calves to be processed for veal. Any extra-label use in food animals is banned by the FDA. Slaughter Withdrawal = 28 days when used as labeled. A withdrawal period has not been established in pre-ruminating calves. *Baytril 100®* (Bayer); (Rx)

HUMAN-LABELED PRODUCTS: None.

Note: Use of enrofloxacin by humans cannot be recommended due to a high degree of CNS effects.

EPHEDRINE SULFATE

(e-*fed*-rin)

SYMPATHOMIMETIC BRONCHODILATOR/ VASOPRESSOR

Prescriber Highlights

- Sympathomimetic used primarily for oral treatment of urinary incontinence & topically for nasal uses
- Contraindications: Severe CV disease, especially with arrhythmias
- Caution: Patients with glaucoma, prostatic hypertrophy, hyperthyroidism, diabetes mellitus, cardiovascular disorders or hypertension
- Adverse Effects: CNS stimulation, tachycardia, hypertension, or anorexia
- Excreted into milk, may affect neonates

Uses/Indications

Ephedrine is used chiefly for the treatment of urethral sphincter hypotonus and resulting incontinence in dogs and cats. It has also been used in an attempt to treat nasal congestion and/or bronchoconstriction in small animals. It can also be used parenterally as a pressor agent in the treatment of shock or anesthesia-associated hypotension.

Pharmacology/Actions

While the exact mechanism of ephedrine's actions are undetermined, it is believed that it indirectly stimulates both alpha-, $beta_1$-, $beta_2$-adrenergic receptors by causing the release of norepinephrine. Prolonged use or excessive dosing frequency can deplete norepinephrine from its storage sites and tachyphylaxis (decreased response) may ensue. Tachyphylaxis has not been documented in dogs or cats, however, when used for urethral sphincter hypotonus.

Pharmacologic effects of ephedrine include: increased vasoconstriction, heart rate, coronary blood flow, blood pressure, mild CNS stimulation, and decreased bronchoconstriction, nasal congestion and appetite. Ephedrine can also increase urethral sphincter tone and produce closure of the bladder neck; its principle veterinary indications are as a result of these effects.

Pharmacokinetics

Ephedrine is rapidly absorbed after oral or parenteral administration. Although not confirmed, ephedrine is thought to cross both the blood-brain barrier and the placenta. Ephedrine is metabolized in the liver and excreted unchanged in the urine. Urine pH may significantly alter excretion characteristics. In humans: at urine pH of 5, half-life is about 3 hours; at urine pH of 6.3, half-life is about 6 hours.

Contraindications/Precautions/Warnings

Ephedrine is contraindicated in patients with severe cardiovascular disease, particularly with arrhythmias. Ephedrine should be used with caution in patients with glaucoma, prostatic hypertrophy, hyperthyroidism, diabetes mellitus, cardiovascular disorders or hypertension.

When administered IV, administration rate should not exceed 10 mg/minute (in humans); it is suggested to scale the rate for veterinary patients.

Adverse Effects

Most likely side effects include restlessness, irritability, tachycardia, or hypertension. Anorexia may be a problem in some animals.

Reproductive/Nursing Safety

Ephedrine's effects on fertility, pregnancy or fetal safety are not known. Use with caution during pregnancy. The drug is excreted in milk and may have deleterious effects on nursing animals. 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.*)

Ephedrine is excreted in milk. If ephedrine is absolutely necessary for the dam, consider using milk replacer.

Overdosage/Acute Toxicity

Clinical signs of overdosage may consist of an exacerbation of the adverse effects listed above or, if a very large overdose, severe cardiovascular (hypertension to rebound hypotension, bradycardias to tachycardias, and cardiovascular collapse) or CNS effects (stimulation to coma) can be seen.

If the overdose was recent, empty the stomach using the usual precautions and administer charcoal and a cathartic. Treat clinical signs supportively as they occur.

Drug Interactions

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

- **ALPHA-BLOCKERS** (*e.g.*, **phentolamine**, **prazosin**): May negate the therapeutic effects of ephedrine
- **ANESTHETICS, GENERAL**: An increased risk of arrhythmias developing can occur if ephedrine is administered to patients who have received cyclopropane or a halogenated hydrocarbon anesthetic agent. Propranolol may be administered should these occur.
- **BETA-BLOCKERS**: Concomitant use of ephedrine with beta-blockers may diminish the effects of both drugs
- **DIGOXIN**: An increased risk of arrhythmias may occur if ephedrine is used concurrently with digitalis glycosides.
- **MONAMINE OXIDASE INHIBITORS** (including **amitraz**): Ephedrine should not be given within two weeks of a patient receiving monoamine oxidase inhibitors; severe hypertension, hyperpyrexia possible
- **SYMPATHOMIMETIC AGENTS, OTHER**: Ephedrine should not be administered with other sympathomimetic agents (*e.g.*, **phenylpropanolamine**) as increased toxicity may result
- **RESERPINE**: May reverse the pressor effects of ephedrine
- **THEOPHYLLINE**: Ephedrine may increase the risk for theophylline toxicity
- **TRICYCLIC ANTIDEPRESSANTS**: May decrease the pressor effects of ephedrine
- **URINARY ALKALINIZERS** (*e.g.*, **sodium bicarbonate**, **citrates**, **carbonic anhydrase inhibitors**): May reduce the urinary excretion of ephedrine and prolong its duration of activity. Dosage adjustments may be required to avoid toxic clinical signs.

Laboratory Considerations

- Beta-adrenergic agonists may decrease **serum potassium** concentrations. Clinical relevance is unknown.

Doses

- **DOGS:**

For treatment of bronchospasm:

a) For maintenance therapy: 1–2 mg/kg PO q8–12h (McKiernan 1992)

b) 2 mg/kg PO q8–12h (Bonagura 1994)

For treatment of urinary incontinence responsive to adrenergic drugs:

a) 5–15 mg (total dose) PO q8h (Labato 1994)

b) 1.2 mg/kg PO q8h or 5–15 mg (total dose) PO q8h (Bartges 2003a)

For treatment of hypotension associated with anesthesia:

a) 0.03–0.1 mg/kg IV bolus. Dilute 5 mg in 10 mL of saline and give the lower dosage first as sinus tachycardia may accompany the higher dose. May repeat in 5 minutes after first dose if hypotension does not improve. (Pablo 2003a)

b) 0.1–0.25 mg/kg IV bolus (Mazzaferro 2005)

c) 0.1 mg/kg IV; short (5–15 min) duration of action (Dodam 2005)

- **CATS:**

For treatment of bronchospasm:

a) For emergency treatment 2–5 mg PO (McKiernan 1992)

For treatment of urinary incontinence responsive to adrenergic drugs:

a) 2–4 mg (total dose) PO q8h (Labato 1994)

b) 2–4 mg/kg PO q6–12h or 2–4 mg (total dose) PO q8h (Bartges 2003a)

c) 2–4 mg per cat PO q8–12h (Polzin 2005c)

Monitoring

- Clinical effectiveness
- Adverse effects (see above)

Client Information

- In order for this drug to be effective, it must be administered as directed by the veterinarian; missed doses will negate its effect. It may take several days for the full benefit of the drug to take place.
- Contact veterinarian if the animal demonstrates ongoing changes in behavior (restlessness, irritability) or if incontinence persists or increases.

Chemistry/Synonyms

A sympathomimetic alkaloid, ephedrine sulfate occurs as fine, odorless, white crystals or powder. Approximately 770 mg are soluble in one mL of water. The commercially available injection has a pH of 4.5–7.

Ephedrine sulfate may also be known as ephedrine sulphate.

Storage/Stability/Compatibility

Store ephedrine sulfate products in tight, light resistant containers at room temperature unless otherwise directed.

When used parenterally, ephedrine sulfate is usually administered directly and not diluted.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

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

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.