Laboratory Considerations
No specific concerns noted; see Monitoring

Doses
- **DOGS/CATS:**

For hyperphosphatemia associated with chronic renal failure:

a) In conjunction with a low-phosphorus diet: Initial therapy at 60–90 mg/kg/day, with food or mixed with food, or just prior to each meal. Individualize dose to achieve desired serum phosphorus concentrations. Perform serial serum phosphorus evaluations at 2–4 week intervals. Decrease dose if serum calcium exceeds normal limits; additional aluminum-based phosphate binders should be used if hyperphosphatemia persists. (Polzin, Osborne et al. 2005)

Monitoring
Initially at 10–14 day intervals; once "stable", at 4–6 week intervals:
- Serum phosphorus (after a 12–hour fast)
- Serum ionized calcium

Client Information
- Give with meals; either just before or mixed into food
- The veterinarian may prescribe additional doses to be administered between meals if additional calcium is required, give only with meals unless the veterinarian instructs to do so
- Use of this medication will require ongoing laboratory monitoring

Chemistry/Synonyms
Calcium acetate is a white, odorless, hygroscopic powder that is freely soluble in water and slightly soluble in alcohol. Each gram contains approximately 254 mg of elemental calcium.

Calcium acetate may also be known as: calcii acetas, acetato de calcio, kalcio acetates, kalciumacetat, or kalciumasetaatti, *PhosLo*®.

Storage/Stability
The commercially available tablets, capsules and gelcaps should be stored at room temperature (25°C); excursions are permitted to 15–30°C.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Calcium Acetate Tablets: 667 mg (169 mg elemental calcium); *PhosLo*® (Nabi); (Rx)

Calcium Acetate Capsules: 333.5 mg (half-size; 84.5 mg elemental calcium), 667 mg (169 mg elemental calcium); *PhosLo*® (Nabi); (Rx)

Calcium Acetate Gelcaps: 667 mg (169 mg elemental calcium); *PhosLo*® (Nabi); (Rx)

Calcium EDTA — see Edetate Calcium Disodium

CALCIUM SALTS
CALCIUM GLUCONATE
CALCIUM GLUCEPTATE
CALCIUM CHLORIDE
CALCIUM LACTATE

(kal-*see*-um)

ESSENTIAL CATION NUTRIENT

Prescriber Highlights
- Used to treat or prevent hypocalcemia; or as an oral antacid
- Contraindicated in V-fib or hypercalcemia
- Must NOT give IV too rapidly
- Must monitor therapy carefully depending on condition, etc.
- Drug interactions & incompatibilities prevalent

Uses/Indications
Calcium salts are used for the prevention or treatment of hypocalcemic conditions.

Pharmacology/Actions
Calcium is an essential element that is required for many functions within the body, including proper nervous and musculoskeletal system function, cell membrane and capillary permeability, and activation of enzymatic reactions.

Pharmacokinetics
Calcium is absorbed in the small intestine in the ionized form only. Presence of vitamin D (in active form) and an acidic pH is necessary for oral absorption. Parathormone (parathyroid hormone) increases with resultant increased calcium absorption in calcium deficiency states and decreases as serum calcium levels rise. Dietary factors (high fiber, phytates, fatty acids), age, drugs (corticosteroids, tetracyclines), disease states (steatorrhea, uremia, renal osteodystrophy, achlorhydria), or decreased serum calcitonin levels may all cause reduced amounts of calcium to be absorbed.

After absorption, ionized calcium enters the extracellular fluid and then is rapidly incorporated into skeletal tissue. Calcium administration does not necessarily stimulate bone formation. Approximately 99% of total body calcium is found in bone. Of circulating calcium, approximately 50% is bound to serum proteins or complexed with anions and 50% is in the ionized form. Total serum calcium is dependent on serum protein concentrations. Total serum calcium changes by approximately 0.8 mg/dl for every 1.09 g/dl change in serum albumin. Calcium crosses the placenta and is distributed into milk.

Calcium is eliminated primarily in the feces, contributed by both unabsorbed calcium and calcium excreted into the bile and pancreatic juice. Only small amounts of the drug are excreted in the urine as most of the cation filtered by the glomeruli is reabsorbed by the tubules and ascending loop of Henle. Vitamin D, parathormone, and thiazide diuretics decrease the amount of calcium excreted by the kidneys. Loop diuretics (*e.g.*, furosemide), calcitonin, and somatotropin increase calcium renal excretion.

Contraindications/Precautions/Warnings

Calcium is contraindicated in patients with ventricular fibrillation or hypercalcemia. Parenteral calcium should not be administered to patients with above normal serum calcium levels. Calcium should be used very cautiously in patients receiving digitalis glycosides, or having cardiac or renal disease. Calcium chloride, because it can be acidifying, should be used with caution in patients with respiratory failure, respiratory acidosis, or renal disease.

In dogs, calcium gluconate diluted 1:1 has been regarded as safe to administer subcutaneously for the treatment of primary hypoparathyroidism in the past, but there are now several case reports of severe tissue reactions (pyogranulomatous panniculitis, adipocyte mineralization, etc.) at the injection site; use with caution, particularly when using with calcitriol.

Adverse Effects

Hypercalcemia can be associated with calcium therapy, particularly in patients with cardiac or renal disease; animals should be adequately monitored. Other effects that may be seen include GI irritation and/or constipation after oral administration, mild to severe tissue reactions after IM or SC administration of calcium salts and venous irritation after IV administration. Calcium chloride may be more irritating than other parenteral salts and is more likely to cause hypotension. Too rapid intravenous injection of calcium can cause hypotension, cardiac arrhythmias and cardiac arrest.

Should calcium salts be infused perivascularly, stop the infusion; treatment then may include: infiltrating the affected area with normal saline, corticosteroids administered locally, applying heat and elevating the area, and infiltrating the affected area with 1% procaine and hyaluronidase.

Reproductive/Nursing Safety

Although parenteral calcium products have not been proven safe to use during pregnancy, they are often used before, during, and after parturition in cows, ewes, bitches, and queens to treat parturient paresis secondary to hypocalcemia. 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.*)

Overdosage/Acute Toxicity

Unless other drugs are given concurrently that enhance the absorption of calcium, oral overdoses of calcium containing products are unlikely to cause hypercalcemia. Hypercalcemia can occur with parenteral therapy or oral therapy in combination with vitamin D or increased parathormone levels. Hypercalcemia should be treated by withholding calcium therapy and other calcium elevating drugs (*e.g.*, vitamin D analogs). Mild hypercalcemia generally will resolve without further intervention when renal function is adequate.

More serious hypercalcemia (>12 mg/dl) should generally be treated by hydrating with IV normal saline and administering a loop diuretic (*e.g.*, furosemide) to increase both sodium and calcium excretion. Potassium and magnesium must be monitored and replaced as necessary. ECG should also be monitored during treatment. Corticosteroids, and in humans calcitonin and hemodialysis, have also been employed in treating hypercalcemia.

Drug Interactions

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

- **CALCIUM CHANNEL BLOCKERS** (*e.g.*, **diltiazem, verapamil,** etc.): Intravenous calcium may antagonize the effects of calcium-channel blocking agents
- **DIGOXIN**: Patients on digitalis therapy are more apt to develop arrhythmias if receiving IV calcium—use with caution
- **MAGNESIUM** (**oral**): With oral calcium may lead to increased serum magnesium and/or calcium, particularly in patients with renal failure.
- **MAGNESIUM SULFATE**: Parenteral calcium can neutralize the effects of hypermagnesemia or magnesium toxicity secondary to parenteral magnesium sulfate
- **NEUROMUSCULAR BLOCKERS** (*e.g.*, **tubocurarine, metubine, gallamine, pancuronium, atracurium, and vecuronium**): Parenteral calcium may reverse the effects of nondepolarizing neuromuscular blocking agents; calcium has been reported to prolong or enhance the effects of tubocurarine
- **TETRACYCLINES, FLUOROQUINOLONES** (**oral**): Oral calcium can reduce the amount of tetracyclines or fluoroquinolones absorbed from the GI tract; separate dosages by two hours if possible
- **POTASSIUM SUPPLEMENTS**: Patients receiving both parenteral calcium and potassium supplementation may have an increased chance of developing cardiac arrhythmias—use cautiously
- **THIAZIDE DIURETICS**: Used in conjunction with large doses of calcium may cause hypercalcemia
- **VITAMIN A**: Excessive intake of vitamin A may stimulate calcium loss from bone and cause hypercalcemia.
- **VITAMIN D**: Concurrent use of large doses of vitamin D or its analogs may cause enhanced calcium absorption and induce hypercalcemia

Laboratory Considerations

- **SERUM AND URINARY MAGNESIUM**: Parenteral calcium may cause false-negative results for serum and urinary magnesium when using the Titan yellow method of determination.

Doses

- **DOGS**

For hypocalcemia:

a) Calcium gluconate injection: 94–140 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) For acute hypocalcemia: Calcium gluconate 10% injection: Warm to body temperature and give IV at a rate of 50–150 mg/kg (0.5–1.5 mL/kg) over 20–30 minutes. If bradycardia develops, halt infusion. Following acute crisis, infuse 10–15 mL (of a 10% solution) per kg over a 24–hour period. Long-term therapy may be accomplished by increasing dietary calcium and using vitamin D. Calcium lactate may be given orally at a rate of 0.5–2 g/day. (Seeler and Thurmon 1985)

c) Calcium gluconate 10% 0.5–1.5 mL/kg or calcium chloride 10% 1.5–3.5 mL (total) IV slowly over 15 minutes; monitor heart rate or ECG during infusion. If ST segment elevation or Q-T interval shortening occur, temporarily discontinue infusion and reinstate at a slower rate when resolved. Maintenance therapy is dependent on cause of hypocalcemia. Hypoparathyroidism is treated with vitamin D analogs (refer to DHT monograph) with or without oral calcium supplementation. (Russo and Lees 1986)

d) For emergency treatment of tetany and seizures secondary to hypoparathyroidism: Calcium gluconate 10%: 0.5–1.5 mL/kg (up to 20 mL) over 15–30 minutes. May repeat at 6–8 hour intervals or give as continuous infusion at 10–15 mg/kg/hour. Monitor ECG and stop infusion if S-T segment elevates, Q-T interval shortens, or arrhythmias occur. For long-term therapy (with DHT—refer to that monograph), calcium

supplementation may occasionally be useful. Calcium gluconate at 500–750 mg/kg/day divided three times daily, or calcium lactate at 400–600 mg/kg/day divided three times daily, or calcium carbonate 100–150 mg/kg/day divided twice daily. Monitor serum calcium and adjust as necessary. (Kay and Richter 1988)

e) For emergency treatment: Calcium gluconate 10% 5–15 mg/kg (0.5–1.5 mL/kg) slowly to effect over a ten minute period, or calcium chloride 10% (extremely caustic if administered extravascularly) 5–15 mg/kg (0.15–0.5 mL/kg); dose is the same but volume is ⅓ that of calcium gluconate; monitor heart rate or ECG (if possible) during infusion. If bradycardia or Q-T interval shortening occurs, temporarily discontinue infusion. Short-term treatment immediately after correction of tetanty: Either give a constant rate infusion of calcium gluconate 10% at 60–90 mg/kg/day (6.5–9.75 mL/kg/day) added to the fluids or give the daily dosage SC in 3–4 divided doses per day after diluting with an equal volume of saline. (Crystal 2004)

For hyperkalemic cardiotoxicity:

a) Secondary to uremic crisis: Correct metabolic acidosis, if present, with sodium bicarbonate (bicarbonate may also be beneficial even if acidosis not present). Calcium gluconate (10%) indicated if serum K+ is >8 mEq/L. Give at an approximate dose of 0.5–1 mL/kg over 10–20 minutes; monitor ECG. Rapidly corrects arrhythmias but effects are very short (10–15 minutes). IV glucose (0.5–1 g/kg body weight with or without insulin) also beneficial in increasing intracellular K+ concentrations. (Polzin and Osborne 1985)

■ CATS:

For hypocalcemia:

a) Calcium gluconate injection: 94–140 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) For acute hypocalcemia secondary to hypoparathyroidism: Using 10% calcium gluconate injection, give 1–1.5 mL/kg IV slowly over 10–20 minutes. Monitor ECG if possible. If bradycardia, or Q-T interval shortening occurs, slow rate or temporarily discontinue. Once life-threatening signs are controlled, add calcium to IV fluids and administer as a slow infusion at 60–90 mg/kg/day (of elemental calcium). This converts to 2.5 mL/kg every 6–8 hours of 10% calcium gluconate. Carefully monitor serum calcium (once to twice daily) during this period and adjust dose as required. Begin oral calcium initially at 50–100 mg/kg/day divided 3–4 times daily of elemental calcium and dihydrotachysterol once animal can tolerate oral therapy. Give DHT initially at 0.125–0.25 mg PO per day for 2–3 days, then 0.08–0.125 mg per day for 2–3 days and finally 0.05 mg PO per day until further dosage adjustments are necessary. As cat's serum calcium is stabilized, intravenous calcium may be reduced and discontinued if tolerated. Stable serum calcium levels (8.5–9.5 mg/dl) are usually achieved in about a week. Continue to monitor and adjust dosages of DHT and calcium to lowest levels to maintain normocalcemia. (Peterson and Randolph 1989) (**Note:** refer to the DHT monograph for further information.)

c) For hypocalcemia secondary to phosphate enema toxicity or puerperal tetany: follow the guidelines for use of intravenous calcium in "b" above. (Peterson and Randolph 1989)

d) For emergency treatment: Calcium gluconate 10% 5–15 mg/kg (0.5–1.5 mL/kg) slowly to effect over a ten minute period, or calcium chloride 10% (extremely caustic if administered extravascularly) 5–15 mg/kg (0.15–0.5 mL/kg); dose is the same but volume is ⅓ that of calcium gluconate; monitor heart rate or ECG (if possible) during infusion. If bradycardia or Q-T interval shortening occurs, temporarily discontinue infusion. Short-term treatment immediately after correction of tetanty: Either give a constant rate infusion of calcium gluconate 10% at 60–90 mg/kg/day (6.5–9.75 mL/kg/day) added to the fluids or give the daily dosage SC in 3–4 divided doses per day after diluting with an equal volume of saline. (Crystal 2004)

■ CATTLE

For hypocalcemia:

a) Calcium gluconate injection: 150–250 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) Calcium gluconate 23% injection: 250–500 mL IV slowly, or IM or SC (divided and given in several locations, with massage at sites of injection) (Label directions; Calcium Gluc. Injection 23%—TechAmerica)

c) 8–12 grams of calcium IV infused over a 5–10 minute period; use a product containing magnesium during the last month of pregnancy if subclinical hypomagnesemia is detected. (Allen and Sansom 1986)

■ HORSES

For hypocalcemia:

a) Calcium gluconate injection: 150–250 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) Calcium gluconate 23% injection: 250–500 mL IV slowly, or IM or SC (divided and given in several locations, with massage at sites of injection) (Label directions; Calcium Gluconate Injection 23%—TechAmerica)

c) For lactation tetany: 250 mL per 450 kg body weight of a standard commercially available solution that also contains magnesium and phosphorous IV slowly while auscultating heart. If no improvement after 10 minutes, repeat. Intensity in heart sounds should be noted, with only an infrequent extrasystole. Stop infusion immediately if a pronounced change in rate or rhythm is detected. (Brewer 1987)

■ SHEEP & GOATS:

For hypocalcemia:

a) Sheep: Calcium gluconate injection: 150–250 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) Sheep: Calcium gluconate 23% injection: 25–50 mL IV slowly, or IM or SC (divided and given in several locations, with massage at sites of injection) (Label directions; Calcium Gluconate Injection 23%—TechAmerica)

■ SWINE:

For hypocalcemia:

a) Calcium gluconate injection: 150–250 mg/kg IV slowly to effect (intraperitoneal route may also be used). Monitor respirations and cardiac rate and rhythm during administration. (USPC 1990)

b) Calcium gluconate 23% injection: 25–50 mL IV slowly, or IM or SC (divided and given in several locations, with massage at sites of injection) (Label directions; Calcium Gluconate Injection 23%—TechAmerica)

■ **BIRDS:**

For hypocalcemic tetany:

a) Calcium gluconate: 50–100 mg/kg IV slowly to effect; may be diluted and given IM if a vein cannot be located (Clubb 1986)

For egg-bound birds:

a) Initially, calcium gluconate 1% solution 0.01–0.02 mL/g IM. Provide moist heat (80–85°F) and allow 24 hours for bird to pass egg. (Nye 1986)

■ **REPTILES:**

For egg binding in combination with oxytocin (oxytocin: 1–10 IU/kg IM.):

a) Calcium glubionate: 10–50 mg/kg IM as needed until calcium levels back to normal or egg binding is resolved. Use care when giving multiple injections. Calcium/oxytocin is not as effective in lizards as in other species. (Gauvin 1993)

Monitoring

- Serum calcium
- Serum magnesium, phosphate, and potassium when indicated
- Serum PTH (parathormone) if indicated
- Renal function tests initially and as required
- ECG during intravenous calcium therapy if possible
- Urine calcium if hypercalcuria develops

Chemistry

Several different salts of calcium are available in various formulations. Calcium gluceptate and calcium chloride are freely soluble in water; calcium lactate is soluble in water; calcium gluconate and calcium glycerophosphate are sparingly soluble in water, and calcium phosphate and carbonate are insoluble in water. Calcium gluconate for injection has a pH of 6–8.2 and calcium chloride for injection has a pH of 5.5–7.5.

To determine calcium content per gram of various calcium salts:

Calcium Acetate: 253 mg (12.7 mEq)
Calcium Carbonate: 400 mg (20 mEq)
Calcium Chloride: 270 mg (13.5 mEq)
Calcium Citrate: 211 mg (10.6 mEq)
Calcium Gluceptate: 82 mg (4.1 mEq)
Calcium Gluconate: 90 mg (4.5 mEq)
Calcium Glycerophosphate: 191 mg (9.6 mEq)
Calcium Lactate: 130 mg (6.5 mEq)
Calcium Phosphate Dibasic
Anhydrous: 290 mg (14.5 mEq)
Dihydrate: 230 mg (11.5 mEq)
Calcium Phosphate Tribasic: 400 mg (20 mEq)

Storage/Stability/Compatibility

Calcium gluconate tablets should be stored in well-closed containers at room temperature. Calcium lactate tablets should be stored in tight containers at room temperature. Calcium gluconate injection, calcium gluceptate injection, and calcium chloride injection should be stored at room temperature and protected from freezing.

Calcium chloride for injection is reportedly **compatible** with the following intravenous solutions and drugs: amikacin sulfate, ascorbic acid, bretylium tosylate, cephapirin sodium, chloramphenicol sodium succinate, dopamine HCl, hydrocortisone sodium succinate, isoproterenol HCl, lidocaine HCl, methicillin sodium, norepinephrine bitartrate, penicillin G potassium/sodium, pentobarbital sodium, phenobarbital sodium, sodium bicarbonate, verapamil HCl, and vitamin B-complex with C.

Calcium chloride for injection **compatibility information conflicts** or is dependent on diluent or concentration factors with the following drugs or solutions: fat emulsion 10%, dobutamine HCl, oxytetracycline HCl, and tetracycline HCl. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used.

Calcium chloride for injection is reportedly **incompatible** with the following solutions or drugs: amphotericin B, cephalothin sodium, and chlorpheniramine maleate.

Calcium gluconate for injection is reportedly **compatible** with the following intravenous solutions and drugs: sodium chloride for injection 0.9%, lactated Ringer's injection, dextrose 5%–20%, dextrose-lactated Ringer's injection, dextrose-saline combinations, amikacin sulfate, aminophylline, ascorbic acid injection, bretylium tosylate, cephapirin sodium, chloramphenicol sodium succinate, corticotropin, dimenhydrinate, erythromycin gluceptate, heparin sodium, hydrocortisone sodium succinate, lidocaine HCl, methicillin sodium, norepinephrine bitartrate, penicillin G potassium/sodium, phenobarbital sodium, potassium chloride, tobramycin sulfate, vancomycin HCl, verapamil and vitamin B-complex with C.

Calcium gluconate compatibility information conflicts or is dependent on diluent or concentration factors with the following drugs or solutions: phosphate salts, oxytetracycline HCl, prochlorperazine edisylate, and tetracycline HCl. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used.

Calcium gluconate is reportedly **incompatible** with the following solutions or drugs: intravenous fat emulsion, amphotericin B, cefamandole naftate, cephalothin sodium, dobutamine HCl, methylprednisolone sodium succinate, and metoclopramide HCl.

Consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-APPROVED PRODUCTS:

(not necessarily a complete list)

Parenteral Products:

Calcium Gluconate (as calcium borogluconate) 23% [230 mg/mL; 20.7 mg (1.06 mEq) calcium per mL]; in 500 mL bottles; *AmTech® Calcium Gluconate 23% Solution* (Phoenix Scientific); (OTC), *Calcium Gluconate 23%* (AgriPharm, AgriLabs, Aspen, Bimeda, Durvet, Phoenix Pharmaceutical, Vet Tek, Vetus); (OTC), *Cal-Nate 1069®* (Butler); (OTC). Depending on the product, approved for use in cattle, horses, swine, sheep, cats, and dogs. No withdrawal times are required.

Calcium Gluconate oral 40 g–42 g calcium/300 mL tube. Supplement for use pre and post calving. *Cal Supreme Gel®* (Bimeda); (OTC)

Calcium Chloride 35% w/w or 47% w/v equivalent to 170 mg calcium/mL (127 mg per gm) in 300 mL (400 g) tube. *Clearcal 50®* (Vedco); (OTC)

Products are also available that include calcium, phosphorus, potassium and/or dextrose; refer to the individual product's labeling for specific dosage information. Trade names for these products include: *Norcalciphos®*—Pfizer, and *Cal-Dextro® Special, #2, C, and K*—Fort Dodge; (Rx).

Oral Products: No products containing only calcium (as a salt) are available commercially with veterinary labeling. There are several products (*e.g.*, *Pet-Cal®* and *Osteoform® Improved*) that contain calcium with phosphorous and vitamin D (plus other ingredients in some preparations).

HUMAN-APPROVED PRODUCTS: (not a complete list)

Parenteral Products:

Calcium Gluconate Injection 10% [100 mg/mL; 9 mg (0.47 mEq) calcium per mL] in 10 mL amps, 10 and 50 mL, 100 mL, and 200 mL vials; generic; (Rx)

Calcium Chloride Injection 10% [100 mg/mL; 27.2 mg (1.36 mEq) calcium per mL] in 10 mL amps, vials, and syringes; generic; (Rx)

Oral Products:

Calcium Gluconate (9.3% calcium) Tablets: 500 mg (45 mg calcium), 650 mg (58.5 mg calcium), 975 mg (87.75 mg calcium), 1 gram (90 mg of calcium); generic; (OTC)

Calcium Lactate (13% calcium) Tablets: 325 mg (42.25 mg calcium), 650 mg (84.5 mg calcium); Capsules (13% calcium), 500 mg (96 mg calcium), *Cal-Lac*® (Bio Tech); generic; (OTC)

Also available are calcium carbonate tablets, suspension and capsules, calcium acetate tablets, calcium citrate tablets, and tricalcium phosphate tablets.

Camphorated Tincture of Opium — See Paregoric

CAPTOPRIL

(***kap***-toe-pril) Capoten®

ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITOR

Prescriber Highlights

- First available ACE inhibitor; use largely supplanted by enalapril & other newer ACE inhibitors
- Shorter duration of activity & more adverse effects than other newer ACE inhibitors

Uses/Indications

The principle uses of captopril in veterinary medicine, at present, are as a vasodilator in the treatment of CHF and in the treatment of hypertension. Because of fewer adverse effects, enalapril and benazepril have largely supplanted the use of this drug in veterinary medicine.

Pharmacology/Actions

Captopril prevents the formation of angiotensin-II (a potent vasoconstrictor) by competing with angiotensin-I for the enzyme angiotensin-converting enzyme (ACE). ACE has a much higher affinity for captopril than for angiotensin-I. Because angiotensin-II concentrations are decreased, aldosterone secretion is reduced and plasma renin activity is increased.

The cardiovascular effects of captopril in patients with CHF include decreased total peripheral resistance, pulmonary vascular resistance, mean arterial and right atrial pressures, and pulmonary capillary wedge pressure; no change or decrease in heart rate; and increased cardiac index and output, stroke volume, and exercise tolerance. Renal blood flow can be increased with little change in hepatic blood flow.

Pharmacokinetics

In dogs, approximately 75% of an oral dose is absorbed but food in the GI tract reduces bioavailability by 30–40%. It is distributed to most tissues (not the CNS) and is 40% bound to plasma proteins in dogs. The half-life of captopril is about 2.8 hours in dogs and less than 2 hours in humans. Its duration of effect in dogs may only persist for 4 hours. The drug is metabolized and renally excreted. More than 95% of a dose is excreted renally, both as unchanged (45–50%) drug and as metabolites. Patients with significant renal dysfunction can have significantly prolonged half-lives.

Contraindications/Precautions/Warnings

Captopril is contraindicated in patients who have demonstrated hypersensitivity with ACE inhibitors. It should be used with caution and under close supervision in patients with renal insufficiency; doses may need to be reduced.

Captopril should also be used with caution in patients with hyponatremia or sodium depletion, coronary or cerebrovascular insufficiency, preexisting hematologic abnormalities or a collagen vascular disease (*e.g.*, SLE).

Patients with severe CHF should be monitored very closely upon initiation of therapy.

Adverse Effects

There have been some reports of hypotension, renal failure, hyperkalemia, vomiting and diarrhea developing in dogs after captopril administration. Captopril may have a higher incidence of gastrointestinal effects in dogs than other available ACE inhibitors. Although seen in people, skin rashes (4–7% incidence) and neutropenia/agranulocytosis (rare) have not been reported in dogs.

Reproductive/Nursing Safety

Captopril apparently crosses the placenta. High doses of ACE inhibitors in rodents have caused decreased fetal weights and increases in fetal and maternal death rates; no teratogenic effects have been reported to date, but use during pregnancy should occur only when the potential benefits of therapy outweigh the risks to the offspring. In humans, the FDA categorizes this drug as category ***C*** for use during the first trimester of 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.*) During the second and third trimesters, the FDA categorizes this drug as category ***D*** for use during pregnancy (*There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***C*** (*These drugs may have potential risks. Studies in people or laboratory animals have uncovered risks, and these drugs should be used cautiously as a last resort when the benefit of therapy clearly outweighs the risks.*)

Captopril enters milk in concentrations of about 1% of that found in maternal plasma.

Overdosage/Acute Toxicity

In overdose situations, the primary concern is hypotension; supportive treatment with volume expansion with normal saline is recommended to correct blood pressure. Dogs given 1.5 gm/kg orally developed emesis and decreased blood pressure. Dogs receiving doses greater than 6.6 mg/kg q8h may develop renal failure.

Drug Interactions

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

- **ANTACIDS:** Reduced oral absorption of captopril may occur if given concomitantly with antacids; it is suggested to separate dosing by at least two hours