- **ANTIDIABETIC AGENTS** (**insulin, oral agents**): Possible increased risk for hypoglycemia; enhanced monitoring recommended
- **DIURETICS** (*e.g.,* **furosemide, hydrochlorothiazide**): Potential for increased hypotensive effects; some veterinary clinicians recommend reducing furosemide doses (by 25–50%) when adding enalapril or benazepril to therapy for heart failure
- **DIURETICS, POTASSIUM-SPARING** (*e.g.,* **spironolactone, triamterene**): Increased hyperkalemic effects, enhanced monitoring of serum potassium
- **LITHIUM**: Increased serum lithium levels possible; increased monitoring required
- **POTASSIUM SUPPLEMENTS**: Increased risk for hyperkalemia

Laboratory Considerations

- When using **iodohippurate sodium I^{123}/I^{134} or Technetium Tc^{99} pententate renal imaging** in patients with renal artery stenosis, ACE inhibitors may cause a reversible decrease in localization and excretion of these agents in the affected kidney which may lead to confusion in test interpretation.

Doses

- **DOGS:**

For adjunctive treatment of heart failure:

a) 0.25–0.5 mg/kg PO once daily (Miller and Tilley 1995); (Trepanier 1999), (Kittleson 2007)

b) 0.25–0.5 mg/kg PO once to twice daily (Ware 1997)

For adjunctive treatment of hypertension:

a) 0.25 mg/kg PO q12h (Brown and Henik 2000)

b) 0.25–0.5 mg/kg q12–24h; Co-administration with a calcium channel antagonist may lower blood pressure when monotherapy is not sufficient. In diabetic dogs, an ACE inhibitor may block adverse effects of calcium channel antagonists. (Brown 2003)

c) For hypertension associated with protein-losing renal disease: 0.5 mg/kg PO once daily (q24h) Response may be variable in dogs with hypertension secondary to other diseases; ACE inhibitors are usually well tolerated and can be tried in non-emergency hypertension. (Stepian 2006a)

- **CATS:**

For adjunctive treatment of heart failure:

a) 0.25–0.5 mg/kg PO once daily (Trepanier 1999), (Kittleson 2007)

b) For CHF or hypertension: 0.25–0.5 mg/kg PO once to twice daily (Atkins 2003b)

For adjunctive treatment of hypertension:

a) 0.5–1 mg/kg PO once daily (Sparkes 2003b)

b) 0.25–1 mg/kg PO once to twice daily. Because of their antiproteinuric effects, ACE inhibitors are the drugs of first choice to treat hypertension in animals with proteinuria. (Langston 2003)

c) 0.25–0.5 mg/kg PO once daily (q24h) (Stepian 2006a)

d) For proteinuria, hypertension associated with chronic kidney disease: 0.25–0.5 mg/kg PO once to twice daily (q12–24h); rarely higher (Polzin 2006)

Monitoring

- Clinical signs of CHF
- Serum electrolytes, creatinine, BUN, urine protein
- Blood pressure (if treating hypertension or clinical signs associated with hypotension arise)

Client Information

- Do not abruptly stop or reduce therapy without veterinarian's approval. Contact veterinarian if vomiting or diarrhea persist or is severe or if animal's condition deteriorates.

Chemistry/Synonyms

Benazepril HCl, an angiotensin converting enzyme inhibitor, occurs as white to off-white crystalline powder. It is soluble in water and ethanol. Benazepril does not contain a sulfhydryl group in its structure.

Benazepril may also be known as: CGS-14824A (benazepril or benazepril hydrochloride), *Benace®, Boncordin®, Briem®, Cibace®, Cibacen®, Cibacen®, Cibacene®, Fortekor®, Labopal®, Lotensin®, Lotrel®, Tensanil®,* or *Zinadril®.*

Storage/Stability/Compatibility

Benazepril tablets (and combination products) should be stored at temperatures less than 86°F (30°C) and protected from moisture. They should be dispensed in tight containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None in the USA

In the UK (and elsewhere): Benazepril Tablets: 2.5, 5, & 20 mg; *Fortekor®* (Novartis—UK); (POM-V) Labeled for use in cats for chronic renal insufficiency and for heart failure in dogs.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Benazepril HCl Tablets: 5 mg, 10 mg, 20 mg, & 40 mg; *Lotensin®* (Novartis); generic; (Rx)

Also available in fixed dose combination products containing amlodipine (*Lotrel®*) or hydrochlorothiazide (*Lotensin HCT®*)

BETAMETHASONE
BETAMETHASONE ACETATE
BETAMETHASONE SODIUM PHOSPHATE

(bet-ta-***meth***-a-sone) Celestone®

GLUCOCORTICOID

Note: For more information on the pharmacology of glucocorticoids refer to the monograph: Glucocorticoids, General information. For topical or otic use, see the Topical Dermatology & Otic sections in the appendix.

Prescriber Highlights

- Injectable (long-acting) & topical glucocorticoid
- Long acting; 25–40X more potent than hydrocortisone; no mineralocorticoid activity
- Goal is to use as much as is required & as little as possible for as short an amount of time as possible
- Primary adverse effects are "Cushingoid" in nature with sustained use
- Many potential drug & lab interactions when used systemically

Contraindications/Precautions/Warnings

For the product *Betasone*® (Schering), the manufacturer states that the drug is "contraindicated in animals with acute or chronic bacterial infections unless therapeutic doses of an effective antimicrobial agent are used." Systemic use of glucocorticoids is generally considered contraindicated in systemic fungal infections (unless used for replacement therapy in Addison's), when administered IM in patients with idiopathic thrombocytopenia and in patients hypersensitive to a particular compound. Use of sustained-release injectable glucocorticoids is contraindicated for chronic corticosteroid therapy of systemic diseases.

Animals that have received glucocorticoids systemically other than with "burst" therapy, should be tapered off the drugs. Patients who have received the drugs chronically should be tapered off slowly as endogenous ACTH and corticosteroid function may return slowly. Should the animal undergo a "stressor" (*e.g.*, surgery, trauma, illness, etc.) during the tapering process or until normal adrenal and pituitary function resume, additional glucocorticoids should be administered.

Corticosteroid therapy may induce parturition in large animal species during the latter stages of pregnancy.

Adverse Effects

Adverse effects are generally associated with long-term administration of these drugs, especially if given at high dosages or not on an alternate day regimen. Effects generally manifest as clinical signs of hyperadrenocorticism. When administered to young, growing animals, glucocorticoids can retard growth. Many of the potential effects, adverse and otherwise, are outlined in the Pharmacology section of the Glucocorticoids, General information monograph.

In dogs, polydipsia (PD), polyphagia (PP) and polyuria (PU), may all be seen with short-term "burst" therapy as well as with alternate-day maintenance therapy on days when given the drug. Adverse effects in dogs associated with long-term use can include: dull, dry haircoat, weight gain, panting, vomiting, diarrhea, elevated liver enzymes, pancreatitis, GI ulceration, lipidemias, activation or worsening of diabetes mellitus, muscle wasting and behavioral changes (depression, lethargy, viciousness). Discontinuation of the drug may be necessary; changing to an alternate steroid may also alleviate the problem. With the exception of PU/PD/PP, adverse effects associated with antiinflammatory therapy are relatively uncommon. Adverse effects associated with immunosuppressive doses are more common and potentially more severe.

Cats generally require higher dosages than dogs for clinical effect but tend to develop fewer adverse effects. Occasionally, polydipsia, polyuria, polyphagia with weight gain, diarrhea, or depression can be seen. Long-term, high dose therapy can lead to "Cushingoid" effects.

Reproductive/Nursing Safety

In addition to the contraindications, precautions and adverse effects outlined above, betamethasone has been demonstrated to cause decreased sperm output and semen volume and increased percentages of abnormal sperm in dogs.

Use with caution in nursing dams. Corticosteroids appear in milk and could suppress growth, interfere with endogenous corticosteroid production or cause other unwanted effects in the nursing offspring. However, in humans, several studies suggest that amounts excreted in breast milk are negligible when prednisone or prednisolone doses in the mother are less than or equal to 20 mg/day or methylprednisolone doses are less than or equal to 8 mg/day. Larger doses for short periods may not harm the infant.

Overdosage/Acute Toxicity

Glucocorticoids when given short-term are unlikely to cause harmful effects, even in massive dosages. One incidence of a dog developing acute CNS effects after accidental ingestion of glucocorticoids has been reported. Should clinical signs occur, use supportive treatment if required.

Chronic usage of glucocorticoids can lead to serious adverse effects. Refer to Adverse Effects above for more information.

Drug Interactions

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

- **AMPHOTERICIN B:** When administered concomitantly with glucocorticoids may cause hypokalemia
- **ANTICHOLINESTERASE AGENTS** (*e.g.*, **pyridostigmine, neostigmine**, etc.): In patients with myasthenia gravis, concomitant glucocorticoid and anticholinesterase agent administration may lead to profound muscle weakness; if possible, discontinue anticholinesterase medication at least 24 hours prior to corticosteroid administration
- **ASPIRIN and OTHER SALICYLATES:** Glucocorticoids may reduce salicylate blood levels
- **BARBITURATES**: May increase the metabolism of glucocorticoids
- **CYCLOPHOSPHAMIDE:** Glucocorticoids may inhibit the hepatic metabolism of cyclophosphamide; dosage adjustments may be required
- **CYCLOSPORINE**: Concomitant administration of glucocorticoids and cyclosporine may increase the blood levels of each by mutually inhibiting hepatic metabolism; clinical significance is not clear
- **DIGOXIN:** When glucocorticoids are used concurrently with digitalis glycosides, an increased chance of digitalis toxicity may occur should hypokalemia develop; diligent monitoring of potassium and digitalis glycoside levels is recommended.
- **DIURETICS, POTASSIUM-DEPLETING** (*e.g.*, **furosemide, thiazides**): When administered concomitantly with glucocorticoids may cause hypokalemia
- **ESTROGENS**: May decrease corticosteroid clearance
- **INSULIN** Requirements may increase in patients receiving glucocorticoids
- **ISONIAZID:** May have serum levels decreased by corticosteroids
- **KETOCONAZOLE:** Corticosteroid clearance may be reduced and the AUC increased
- **MITOTANE:** May alter the metabolism of steroids; higher than usual doses of steroids may be necessary to treat mitotane-induced adrenal insufficiency
- **RIFAMPIN:** May increase the metabolism of glucocorticoids
- **THEOPHYLLINES:** Alterations of pharmacologic effects of either drug can occur
- **ULCEROGENIC DRUGS** (*e.g.*, **NSAIDs**): Use with glucocorticoids may increase the risk of gastrointestinal ulceration
- **VACCINES:** Patients receiving corticosteroids at immunosuppressive dosages should generally not receive live attenuated-virus vaccines as virus replication may be augmented; diminished immune response may occur after vaccine, toxoid, or bacterin administration in patients receiving glucocorticoids

Laboratory Considerations

- Glucocorticoids may increase **serum cholesterol** and **urine glucose** levels
- Glucocorticoids may decrease **serum potassium**

- Glucocorticoids can suppress the release of thyroid stimulating hormone (TSH) and reduce **T_3 & T_4** values; thyroid gland atrophy has been reported after chronic glucocorticoid administration
- Uptake of **I^{131}** by the thyroid may be decreased by glucocorticoids
- Reactions to **skin tests** may be suppressed by glucocorticoids
- False-negative results of the **nitroblue tetrazolium test** for systemic bacterial infections may be induced by glucocorticoids
- Betamethasone does not cross-react with the cortisol assay

Doses

- **DOGS:**

  For the control of pruritus:

  a) *Betasone® Aqueous Suspension*: 0.25–0.5 mL per 20 pounds body weight IM. Dose dependent on severity of condition. May repeat when necessary. Relief averages 3 weeks in duration. Do not exceed more than 4 injections. (Package Insert; *Betasone®*—Schering) **Note:** Product no longer marketed in the USA.

- **HORSES:**

  Source of product an issue. Alternative is triamcinolone (see that monograph for additional information). (**Note:** ARCI UCGFS Class 4 Drug)

  As a relatively short-acting corticosteroid for intraarticular administration:

  a) 6–15 mg per joint IA. Frequency of re-injection is limited to the minimum number needed to achieve soundness. (Frisbee 2003)

Monitoring

Monitoring of glucocorticoid therapy is dependent on its reason for use, dosage, agent used (amount of mineralocorticoid activity), dosage schedule (daily versus alternate day therapy), duration of therapy, and the animal's age and condition. The following list may not be appropriate or complete for all animals; use clinical assessment and judgment should adverse effects be noted:

- Weight, appetite, signs of edema
- Serum and/or urine electrolytes
- Total plasma proteins, albumin
- Blood glucose
- Growth and development in young animals
- ACTH stimulation test if necessary

Client Information

- Clients should carefully follow the dosage instructions and should not discontinue the drug abruptly without consulting veterinarian beforehand
- Clients should be briefed on the potential adverse effects that can be seen with these drugs and instructed to contact the veterinarian should these effects become severe or progress

Chemistry/Synonyms

A synthetic glucocorticoid, betamethason is available as the base and as the dipropionate, acetate and sodium phosphate salts. The base is used for oral dosage forms. The sodium phosphate and acetate salts are used in injectable preparations. The dipropionate salt is used in topical formulations and in combination with the sodium phosphate salt in a veterinary-approved injectable preparation.

Betamethasone occurs as an odorless, white to practically white, crystalline powder. It is insoluble in water and practically insoluble in alcohol. The dipropionate salt occurs as a white or creamy-white, odorless powder. It is practically insoluble in water and sparingly soluble in alcohol. The sodium phosphate salt occurs as an odorless, white to practically white, hygroscopic powder. It is freely soluble in water and slightly soluble in alcohol.

Betamethasone may also be known as flubenisolone or *Celestone®*.

Storage/Stability/Compatibility

Betamethasone tablets should be stored in well-closed containers at 2–30°C. The oral solution should be stored in well-closed containers, protected from light and kept at temperatures less than 40°C. The sodium phosphate injection should be protected from light and stored at room temperature (15–30°C); protect from freezing. The combination veterinary injectable product (*Betasone®*) should be stored between 2–30°C and protected from light and freezing.

When betamethasone sodium phosphate was mixed with heparin sodium, hydrocortisone sodium succinate, potassium chloride, vitamin B-complex with C, dextrose 5% in water (D_5W), D_5 in Ringer's, D_5 in lactated Ringer's, Ringer's lactate injection or normal saline, no physical incompatibility was noted immediately or after 4 hours.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

The following product is apparently no longer marketed in the USA. Betamethasone Diproprionate Injection equivalent to 5 mg/mL of betamethasone and betamethasone sodium phosphate equivalent to 2 mg/mL betamethasone in 5 mL vials; *Betasone®* (Schering-Plough); (Rx). Approved for use in dogs.

Betamethasone valerate is also found in *Gentocin® Otic*, *Gentocin® Topical Spray* and *Topagen® Ointment*, (Schering-Plough). There are several other otic and topical products containing betamethasone and gentamicin on the veterinary market. See the appendix for more information on these products.

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Betamethasone Tablets: 0.6 mg; *Celestone®* (Schering); (Rx)

Betamethasone Solution: 0.6 mg/5 mL in 118 mL; *Celestone®* (Schering); (Rx)

Betamethasone Injection: betamethasone (as sodium phosphate) 3 mg/mL and betamethasone acetate 3 mg/mL injection in 5 mL vials; *Celestone Soluspan®* (Schering); (Rx)

BETHANECHOL CHLORIDE

(beh-***than***-e-kole) Urecholine®

CHOLINERGIC

Prescriber Highlights

- Cholinergic agent used primarily to increase bladder contractility; symptomatic treatment of dysautonomia
- Principle contraindications are GI or urinary tract obstructions or if bladder wall integrity is in question
- Adverse Effects: "SLUD" (salivation, lacrimation, urination, defecation)
- Cholinergic crisis possible if injecting IV or SC, have atropine at the ready