Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Detomidine HCl for Injection: 10 mg/mL in 5 and 20 mL vials; *Dormosedan*® (Pfizer); (Rx). Approved for use in mature horses and yearlings.

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

HUMAN-LABELED PRODUCTS: None

DEXAMETHASONE DEXAMETHASONE SODIUM PHOSPHATE

(dex-a-*meth*-a-zone) Azium®, Dexasone®

GLUCOCORTICOID

Prescriber Highlights

- Injectable, oral & ophthalmic glucocorticoid
- Long acting; 30X more potent than hydrocortisone; no mineralocorticoid activity
- If using for therapy, 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

Uses/Indications

Glucocorticoids have been used in an attempt to treat practically every malady that afflicts man or animal, but there are three broad uses and dosage ranges for use of these agents. 1) Replacement of glucocorticoid activity in patients with adrenal insufficiency, 2) as an antiinflammatory agent, and 3) as an immunosuppressive. Among some of the uses for glucocorticoids include treatment of: endocrine conditions (*e.g.*, adrenal insufficiency), rheumatic diseases (*e.g.*, rheumatoid arthritis), collagen diseases (*e.g.*, systemic lupus), allergic states, respiratory diseases (*e.g.*, asthma), dermatologic diseases (*e.g.*, pemphigus, allergic dermatoses), hematologic disorders (*e.g.*, thrombocytopenias, autoimmune hemolytic anemias), neoplasias, nervous system disorders (increased CSF pressure), GI diseases (*e.g.*, ulcerative colitis exacerbations), and renal diseases (*e.g.*, nephrotic syndrome). Some glucocorticoids are used topically in the eye and skin for various conditions or are injected intra-articularly or intralesionally. The above listing is certainly not complete. For specific dosages and indications refer to the Doses section.

High dose dexamethasone use for shock or CNS trauma is controversial; recent studies have not demonstrated significant benefit and it actually may cause increased deleterious effects.

Pharmacology/Actions

Glucocorticoids have effects on virtually every cell type and system in mammals. An overview of the effects of these agents follows:

CARDIOVASCULAR SYSTEM: Glucocorticoids can reduce capillary permeability and enhance vasoconstriction. A relatively clinically insignificant positive inotropic effect can occur after glucocorticoid administration. Increased blood pressure can result from both the drugs' vasoconstrictive properties and increased blood volume that may be produced.

CELLS: Glucocorticoids inhibit fibroblast proliferation, macrophage response to migration inhibiting factor, sensitization of lymphocytes and the cellular response to mediators of inflammation. Glucocorticoids stabilize lysosomal membranes.

CNS/AUTONOMIC NERVOUS SYSTEM: Glucocorticoids can lower seizure threshold, alter mood and behavior, diminish the response to pyrogens, stimulate appetite and maintain alpha rhythm. Glucocorticoids are necessary for normal adrenergic receptor sensitivity.

ENDOCRINE SYSTEM: When animals are not stressed, glucocorticoids will suppress the release of ACTH from the anterior pituitary, thereby reducing or preventing the release of endogenous corticosteroids. Stress factors (*e.g.*, renal disease, liver disease, diabetes) may sometimes nullify the suppressing aspects of exogenously administered steroids. Release of thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), prolactin, and luteinizing hormone (LH) may all be reduced when glucocorticoids are administered at pharmacological doses. Conversion of thyroxine (T_4) to triiodothyronine (T_3) may be reduced by glucocorticoids; plasma levels of parathyroid hormone increased. Glucocorticoids may inhibit osteoblast function. Vasopressin (ADH) activity is reduced at the renal tubules and diuresis may occur. Glucocorticoids inhibit insulin binding to insulin-receptors and the post-receptor effects of insulin.

HEMATOPOIETIC SYSTEM: Glucocorticoids can increase the numbers of circulating platelets, neutrophils and red blood cells, but platelet aggregation is inhibited. Decreased amounts of lymphocytes (peripheral), monocytes and eosinophils are seen as glucocorticoids can sequester these cells into the lungs and spleen and prompt decreased release from the bone marrow. Removal of old red blood cells becomes diminished. Glucocorticoids can cause involution of lymphoid tissue.

GI TRACT AND HEPATIC SYSTEM: Glucocorticoids increase the secretion of gastric acid, pepsin, and trypsin. They alter the structure of mucin and decrease mucosal cell proliferation. Iron salts and calcium absorption are decreased while fat absorption is increased. Hepatic changes can include increased fat and glycogen deposits within hepatocytes, increased serum levels of alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (GGT). Significant increases can be seen in serum alkaline phosphatase levels. Glucocorticoids can cause minor increases in BSP (bromosulfophthalein) retention time.

IMMUNE SYSTEM (also see Cells and Hematopoietic System): Glucocorticoids can decrease circulating levels of T-lymphocytes; inhibit lymphokines; inhibit neutrophil, macrophage, and monocyte migration; reduce production of interferon; inhibit phagocytosis and chemotaxis; antigen processing; and diminish intracellular killing. Specific acquired immunity is affected less than nonspecific immune responses. Glucocorticoids can also antagonize the complement cascade and mask the clinical signs of infection. Mast cells are decreased in number and histamine synthesis is suppressed. Many of these effects only occur at high or very high doses and there are species differences in response.

METABOLIC EFFECTS: Glucocorticoids stimulate gluconeogenesis. Lipogenesis is enhanced in certain areas of the body (*e.g.*, abdomen) and adipose tissue can be redistributed away from the extremities to the trunk. Fatty acids are mobilized from tissues and their oxidation is increased. Plasma levels of triglycerides, cholesterol, and glycerol are increased. Protein is mobilized from most areas of the body (not the liver).

MUSCULOSKELETAL: Glucocorticoids may cause muscular weakness (also caused if there is a lack of glucocorticoids), atrophy, and osteoporosis. Bone growth can be inhibited via growth hormone and somatomedin inhibition, increased calcium excretion and inhibition of vitamin D activation. Resorption of bone can be enhanced. Fibrocartilage growth is also inhibited.

OPHTHALMIC: Prolonged corticosteroid use (both systemic or topically to the eye) can cause increased intraocular pressure and glaucoma, cataracts, and exophthalmos.

RENAL, FLUID, & ELECTROLYTES: Glucocorticoids can increase potassium and calcium excretion, sodium and chloride reabsorption, and extracellular fluid volume. Hypokalemia and/or hypocalcemia rarely occur. Diuresis may develop following glucocorticoid administration.

SKIN: Thinning of dermal tissue and skin atrophy can be seen with glucocorticoid therapy. Hair follicles can become distended and alopecia may occur.

Pharmacokinetics

Pharmacokinetics of dexamethasone do not translate into pharmacologic effect. The half-life of dexamethasone in dogs is about 2–5 hours, but biologic activity can persist for 48 hours or more.

Contraindications/Precautions/Warnings

Because dexamethasone has negligible mineralocorticoid effect, it should generally not be used alone in the treatment of adrenal insufficiency.

Do not administer the propylene glycol base injectable product rapidly intravenously; hypotension, collapse, and hemolytic anemia can occur. Many clinicians only use dexamethasone sodium phosphate when giving the drug intravenously.

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 considered 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.

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 are manifested as clinical signs of hyperadrenocorticism. Glucocorticoids can retard growth in young animals. Many of the potential effects, adverse and otherwise, are outlined above in the Pharmacology section.

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 giving the drug. Adverse effects in dogs 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, however.

Administration of dexamethasone or triamcinolone may play a role in the development of laminitis in horses.

Reproductive/Nursing Safety

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

Overdosage/Acute Toxicity

Glucocorticoids when given short-term are unlikely to cause significant 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 dexamethasone and may be of significance in veterinary patients:

- **AMPHOTERICIN B:** 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:** Glucocorticoids may reduce salicylate blood levels
- **BARBITURATES:** May increase the metabolism of glucocorticoids and decrease dexamethasone blood levels
- **CYCLOPHOSPHAMIDE:** Glucocorticoids may also 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 the hepatic metabolism of each other; the clinical significance of this interaction is not clear
- **DIAZEPAM:** Dexamethasone may decrease diazepam levels

- **DIURETICS, POTASSIUM-DEPLETING** (*e.g.*, **spironolactone, triamterene**): Administered concomitantly with glucocorticoids may cause hypokalemia
- **EPHEDRINE:** May reduce dexamethasone blood levels and interfere with dexamethasone suppression tests
- **INDOMETHACIN:** Can cause false negative test results in the dexamethasone suppression test
- **INSULIN:** Insulin requirements may increase in patients receiving glucocorticoids
- **KETOCONAZOLE AND OTHER AZOLE ANTIFUNGALS:** May decrease the metabolism of glucocorticoids and increase dexamethasone blood levels; ketoconazole may induce adrenal insufficiency when glucocorticoids are withdrawn by inhibiting adrenal corticosteroid synthesis
- **MACROLIDE ANTIBIOTICS** (**erythromycin, clarithromycin**): May decrease the metabolism of glucocorticoids and increase dexamethasone blood levels
- **MITOTANE:** May alter the metabolism of steroids; higher than usual doses of steroids may be necessary to treat mitotane-induced adrenal insufficiency
- **NSAIDS:** Administration of ulcerogenic drugs with glucocorticoids may increase the risk of gastrointestinal ulceration
- **PHENYTOIN:** May increase the metabolism of glucocorticoids and decrease dexamethasone blood levels
- **RIFAMPIN:** May increase the metabolism of glucocorticoids and decrease dexamethasone blood levels
- **VACCINES:** Patients receiving corticosteroids at immunosuppressive dosages should generally not receive live attenuated-virus vaccines as virus replication may be augmented; a diminished immune response may occur after vaccine, toxoid, or bacterin administration in patients receiving glucocorticoids

Laboratory Considerations

- Glucocorticoids may increase **serum cholesterol**
- Glucocorticoids may increase **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
- Glucocorticoids may cause **neutrophilia** within 4–8 hours after dosing and return to baseline within 24–48 hours after drug discontinuation
- Glucocorticoids can cause **lymphopenia** in dogs which can persist for weeks after drug discontinuation

Doses

- **DOGS:**

For labeled indications (antiinflammatory; glucocorticoid agent):

a) Injection: 0.5–1 mg IV or IM; may be repeated for 3–5 days; Tablets: 0.25–1.25 mg PO daily in single or two divided doses (Package Insert; *Azium®*— Schering)

Low-Dose Dexamethasone Suppression Test:

a) Draw pre-sample. Inject 0.01–0.015 mg/kg dexamethasone IV (may dilute dexamethasone 1:10 with sterile saline to insure accurate dosing). Collect samples at 4 hrs. and 8 hrs. post dexamethasone. Usual pre-dose cortisol normals: 0.5–4.0 micrograms/dl; post-dexamethasone normals: less than 1.5 micrograms/dl (Kemppainen and Zerbe 1989a)

b) Draw pre-sample in AM. Inject 0.01 mg/kg dexamethasone sodium phosphate IV. Draw sample 8 hours post injection. (Feldman 1989), (Morgan 1988), (Feldman, Schrader, and Twedt 1988)

High-Dose Dexamethasone Suppression Test:

a) Draw pre-dose sample. Inject 0.1 or 1 mg/kg IV dexamethasone. Draw post-dose samples at 4 hours and 8 hours. Use 1 mg/kg dose if not suppressed at lower dose (0.1 mg/kg). Use 1 mg/kg dose with caution in patients with diabetes mellitus and if cortisol values are greater than 12 micrograms/dl (Kemppainen and Zerbe 1989a)

b) Draw pre-dose sample. Administer 0.1 mg/kg IV dexamethasone sodium phosphate. Draw second sample 8 hours post injection (Feldman 1989)

c) Draw pre-dose sample. Administer 0.1 mg/kg IV dexamethasone sodium phosphate. Draw second sample 4 hours post injection (Morgan 1988)

d) Draw pre-dose sample. Administer 0.1 mg/kg IV dexamethasone sodium phosphate. Draw second sample 4 or 8 hours post injection (Feldman, Schrader, and Twedt 1988)

Combined Dexamethasone Suppression-ACTH Stimulation test:

a) Draw pre-dose sample. Administer 0.1 mg/kg IV dexamethasone; collect post-dexamethasone sample 4 hours later. Immediately give ACTH (gel) 2.2 IU/kg IM. Collect post-ACTH sample 2 hours later. (Kemppainen and Zerbe 1989a)

For tentative diagnosis of Addison's disease:

a) 1) Draw blood for hemogram, serum biochemistry and basal cortisol; 2) Begin IV fluids and give 2–5 mg/kg dexamethasone sodium phosphate; 3) Immediately give 0.25 mg of cosyntropin IV or IM; 4) Draw a second blood sample for plasma cortisol 45–60 minutes later. Blood levels of <1 mcg/dL are typical for hypoadrenocorticism, while those stimulating to only 2–3 mcg/dL are also suggestive. (Schaer 2006)

For toy breed dogs with hydrocephalus:

a) 0.25 mg/kg three to four times daily; reduce dose slowly over 2–4 weeks (Simpson 1989)

For adjunctive therapy of craniocerebral/spinal trauma:

a) If patient's condition is not improved 30 minutes after receiving water-soluble glucocorticoids: 2 mg/kg by slow IV infusion. If patient continues to deteriorate, additional therapy is warranted. (Shores 1989)

b) Initially, 0.2 mg/kg bolus, then 0.2 mg/kg daily in 2–3 divided doses. If animal is in shock, give 2 mg/kg initially. (Fenner 1986a)

c) For spinal cord trauma: 2–3 mg/kg IV followed in 6–8 hours by 1 mg/kg SC or IV two to three times daily for 24 hours. Then 0.2 mg/kg SC or IV two to three times daily for 2–3 days. Then 0.1 mg/kg IV or SC two to three times daily for 3–5 days (Schunk 1988a)

To reduce intracerebral pressure and edema:

a) In the palliative therapy of intracranial neoplasms: 0.25–2 mg/kg q6h IV in acute episodes (LeCouteur and Turrel 1986)

b) In the adjunctive therapy of status epilepticus: 2 mg/kg IV initially; repeat in 6–8 hours with 1 mg/kg. Follow with tapering doses. (Schunk 1988b)

For adjunctive therapy of fibrocartilaginous embolic myopathy:
a) 2.2 mg/kg IV, then 6–8 hours later give 1 mg/kg SC. Repeat 1 mg/kg SC in 12 hours, then give 0.1 mg/kg SC twice daily for 3–5 days (Schunk 1988a)

For patients with thoracolumbar intervertebral disk disease and acute onset of paraparesis:
a) 2 mg/kg IV followed in 6–8 hours with 0.5–1 mg/kg SC, two to three times daily for 24 hours, then 0.1 mg/kg SC or PO twice daily for 3–5 days (Schunk 1988a)

For medical therapy of cervical spondylopathy:
a) With an acute onset or sudden worsening with moderate to marked tetraparesis: 2.2 mg/kg IV once followed in 6–8 hours by 1 mg/kg SC twice daily for two doses. Then 0.1–0.2 mg/kg PO or SC twice a day for 3–5 days (Schunk 1988a)

For adjunctive therapy of shock:
a) Dexamethasone sodium phosphate: 4–6 mg/kg IV (Kemppainen 1986)

For initial adjunctive treatment of acute adrenocortical collapse:
a) Dexamethasone: 0.5–1 mg/kg IV or Dexamethasone Sodium phosphate 2–4 mg/kg IV (Schrader 1986), (Feldman, Schrader, and Twedt 1988)

For treatment of acquired thrombocytopenia:
a) 0.25–0.3 mg/kg IV or SC once, then 0.1–0.15 mg/kg SC or PO twice a day for 7 days. Decrease oral dose by ½ every 5–7 days for 3 weeks, then go to alternate day therapy for 6 weeks. (Dodds 1988)

For adjunctive therapy of endotoxemia secondary to acute gastric dilatation-volvulus:
a) 5 mg/kg slowly IV (Bellah 1988)

For adjunctive therapy of cholecalciferol (*Quintox®*, *Rampage®*) toxicity:
a) 1 mg/kg SC divided four times daily (Grauer and Hjelle 1988b)

■ **CATS:**

For labeled indications (antiinflammatory; glucocorticoid agent):
a) Injection: 0.125–0.5 mg IV or IM; may be repeated for 3–5 days; Tablets: 0.125–0.5 mg daily in single or divided doses (Package Insert; *Azium®*— Schering)

High-Dose Dexamethasone Suppression Test:
a) As a screening test for feline hyperadrenocorticism: 0.1 mg/kg IV. A dose of 1 mg/kg IV may differentiate pituitary-dependent hyperadrenocorticism (PDH) from an adrenal tumor. (Zerbe 1989)

Combined Dexamethasone Suppression-ACTH Stimulation Test:
a) Collect blood sample, then give dexamethasone 0.1 mg IV, collect sample 2 hours after dexamethasone. Immediately give ACTH (2.2 IU/kg) and collect samples 1 and 2 hours post ACTH. (Zerbe 1989)

For endotoxic or septicemic shock:
a) Dexamethasone sodium succinate: 5 mg/kg IV (Jenkins 1985)

As adjunctive therapy for feline neoplasias (lymphosarcoma, acute lymphoid leukemia, mast cell neoplasms):
a) 2–6 mg/m2 q24–48h PO, SC or IV (Couto 1989)

For adjunctive emergency treatment of feline asthma:
a) 1 mg/kg IV (sodium phosphate salt) (Noone 1986)

For chronic therapy of feline allergic bronchitis:
a) 0.25 mg PO one to three times daily. Once patient stabilizes, attempt to reduce dose; keep on alternate-day therapy for at least 1–2 months after symptoms have initially resolved. (Bauer 1988)

For alternative therapy for idiopathic feline miliary dermatitis:
a) 1 mg PO once daily for 7 days, then 1 mg PO twice a week. May need to add progestational agent. (Kwochka 1986)

■ **RABBITS/RODENTS/SMALL MAMMALS:**
a) Mice, Rats, Gerbils, Hamsters, Guinea pigs, Chinchillas: 0.6 mg/kg IM (as an antiinflammatory) (Adamcak and Otten 2000)

■ **CATTLE:**

For adjunctive therapy of insect bites or stings:
a) 2 mg/kg IM or IV q4h (use epinephrine if anaphylaxis develops) (Fowler 1993)

For adjunctive therapy of cerebral edema secondary to polioencephalomalacia:
a) 1–2 mg/kg intravenously (Dill 1986)

For adjunctive therapy of radial nerve injury, or femoral nerve paralysis:
a) Adult cattle (400–800 kg and not pregnant): 20–40 mg IM or IV; Calves: 10 mg IM or IV. Taper or discontinue therapy in 2–3 days. Many cases require only a single dose. (Rebhun 1986)

For adjunctive therapy of obturator nerve paralysis:
a) 10–40 mg parenterally once daily for 2–3 days, then discontinue (Rebhun 1986)

For adjunctive therapy of peroneal nerve injuries:
a) 10–30 mg parenterally for acute cases when not contraindicated due to pregnancy or infection (Rebhun 1986)

For elective inducement of parturition or termination of pregnancy:
a) For abortion: 25 mg parenterally with 25 mg prostaglandin F_{2alpha} after 150 days of gestation. For inducement or parturition from 8th month of gestation on: 20 mg IM. (Drost 1986)
b) For inducement of parturition when given within 2 weeks of normal term: 20–30 mg IM (Barth 1986)

For adjunctive therapy of aseptic laminitis:
a) 5–20 mg IM or IV; continue therapy for 2–3 days (Berg 1986)

For primary bovine ketosis:
a) 5–20 mg IV or IM (Package Insert; *Azium®*— Schering)

■ **HORSES:** (**Note:** ARCI UCGFS Class 4 Drug)

For labeled indications (antiinflammatory; glucocorticoid agent):
a) Dexamethasone Injection: 2.5–5 mg IV or IM (Package Insert; *Azium®*— Schering)

Dexamethasone sodium phosphate injection: 2.5–5 mg IV (Package Insert; *Azium® SP*— Schering)

For recurrent airway obstruction (heaves):
a) For a 500 kg horse give 40 mg IM once every other day for 3 treatments, followed by 35 mg IM once every other day for 3 treatments, followed by 30 mg IM once every other day for 3 treatments, etc., until horse is weaned off dexamethasone. Corticosteroid use may be contraindicated in horses predisposed to laminitis or exhibiting endocrinopathies. (Ainsworth and Hackett 2004)

For glucocorticoid therapy:
a) 0.05–0.2 mg/kg once daily IV, IM or PO (Robinson 1987)

Dexamethasone suppression test:
a) 20 mg IM. Normal values: Cortisol levels decrease 50% in 2 hours, 70% in 4 hours, and 80% at 6 hours. At 24 hours, levels are still depressed about 30% of original value. (Beech 1987b)

■ **SWINE:**

For glucocorticoid therapy:

a) 1–10 mg IV or IM (Howard 1986)

■ **LLAMAS:**

For adjunctive therapy of anaphylaxis:

a) 2 mg/kg IV (Smith 1989)

■ **BIRDS:**

For shock, trauma, gram-negative endotoxemia:

a) Dexamethasone 2 mg/mL injection: 2–4 mg/kg IM or IV once, twice or three times daily. Taper off drug when using long-term. (Clubb 1986)

■ **REPTILES:**

For septic shock in most species:

a) Using Dexamethasone Sodium Phosphate: 0.1–0.25 mg/kg IV or IM (Gauvin 1993)

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 with 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, dexamethasone occurs as an odorless, white to practically white, crystalline powder that melts with some decomposition at about 250°C. It is practically insoluble in water and sparingly soluble in alcohol. Dexamethasone sodium phosphate occurs as an odorless or having a slight odor, white to slightly yellow, hygroscopic powder. One gram is soluble in about 2 mL of water; it is slightly soluble in alcohol

1.3 mg of dexamethasone sodium phosphate is equivalent to 1 mg of dexamethasone; 4 mg/mL of dexamethasone sodium phosphate injection is approximately equivalent to 3 mg/mL of dexamethasone.

Dexamethasone may also be known as: desamethasone, dexametasone, dexamethasonum, 9alpha-Fluoro-16alpha-methylprednisolone; hexadecadrol; many trade names are available.

Storage/Stability/Compatibility

Dexamethasone is heat labile and should be stored at room temperature (15–30°C) unless otherwise directed by the manufacturer. Dexamethasone sodium phosphate injection should be protected from light. Dexamethasone tablets should be stored in well-closed containers.

Dexamethasone sodium phosphate for injection is reportedly **compatible** with the following drugs: amikacin sulfate, aminophylline, bleomycin sulfate, cimetidine HCl, glycopyrrolate, lidocaine HCl, nafcillin sodium, netilmicin sulfate, prochlorperazine edisylate and verapamil.

Dexamethasone sodium phosphate is reportedly **incompatible** with: daunorubicin HCl, doxorubicin HCl, metaraminol bitartrate, and vancomycin. 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:

Dexamethasone Injection: 2 mg/mL; *Amtech® Dexamethasone Solution* (Phoenix Scientific), *Azium® Solution* (Schering-Plough), Dexamethasone 2 mg Injection (Vedco, RXV), Dexamethasone Injection (Bimeda, ProLabs, Vet Tek, Dexamethasone Solution (Aspen, Butler, Phoenix Pharmaceutical), *Dexasone®* (RXV); (Rx). Approved for use in dogs, cats, horses (those not intended for food) and cattle. There are no withdrawal times required when used in cattle. A withdrawal period has not been established for this product in preruminal calves; do not use in veal calves.

Dexamethasone Oral Powder: 10 mg crystalline in 10 mg packets. Approved for use in cattle and horses (not horses intended for food). *Azium® Powder* (Schering-Plough); (Rx)

Dexamethasone Sodium Phosphate Injection: 4 mg/mL (equivalent to 3 mg/mL dexamethasone); *Dexaject SP®* (Vetus), Dexamethasone Sodium Phosphate Injection (Butler, Vedco); generic; (Rx). Approved for use in horses.

Dexamethasone 5 mg and trichlormethiazide 200 mg oral bolus: in boxes of 30 and 100 boluses; *Naquasone® Bolus* (Schering-Plough); (Rx). Approved for use in cattle. Milk withdrawal = 72 hours.

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

HUMAN-LABELED PRODUCTS:

Dexamethasone Tablets: 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, & 6 mg; *Decadron®* (Merck); generic; (Rx)

Dexamethasone Oral Elixir/Solution: 0.5 mg/5 mL in 100 mL, 237 mL, 500 mL and UD 5 and UD 20 mL, 1 mg/mL (concentrate) in 30 mL with dropper; *Dexamethasone Intensol®* (Roxane); generic; (Rx)

Dexamethasone Sodium Phosphate Injection: 4 mg/mL (as sodium phosphate solution) in 1, 5, 10 and 30 mL vials, 1 mL syringe and 1 mL fill in 2 mL vials; generic; (Rx); 10 mg/mL (as sodium phosphate solution) in 1mL and 10 mL vials and 1 mL syringes; generic; (Rx); 20 mg/mL (as sodium phosphate solution) in 5 mL vials (IV) (with sodium sulfite & benzyl alcohol); *Hexadrol® Phosphate* (Organon), (Rx)

Dexamethasone is also available in topical ophthalmic (see ophthalmic products in the appendix) and inhaled aerosol dosage forms.

DEXMEDETOMIDINE

(deks-mee-deh-*toe*-mih-deen) Dexdomitor®

ALPHA-2 ADRENERGIC AGONIST

Prescriber Highlights

- Alpha-2 agonist similar to medetomidine used as a pre-anesthetic & for sedation, analgesia in dogs & cats
- Contraindications: cardiac disease, liver or kidney diseases, shock, severe debilitation, or animals stressed due to heat, cold or fatigue; caution in very old or young animals, animals with seizure disorders, respiratory, renal or kidney disorders
- Adverse Effects: Bradycardia, occasional AV blocks, decreased respiration, hypothermia, urination, vomiting, hyperglycemia, & pain on injection (IM). Rarely: prolonged sedation, paradoxical excitation, hypersensitivity, apnea & death from circulatory failure
- Dosed in dogs based upon body surface area, not weight
- Effects may be reversed with atipamezole

Note: *This compound has been approved for use in dogs in the USA, but at the time of writing (Autumn 2007) it had not yet been marketed in the USA and the package insert was not available for review. The following should be considered a preliminary monograph.*

Uses/Indications

In the USA, dexmedetomidine for dogs is approved for use as a sedative and analgesic to facilitate clinical examinations, clinical procedures, minor surgical procedures, and minor dental procedures, and as a preanesthetic to general anesthesia.

In Europe, dexmedetomidine is additionally indicated for use in cats similarly to dogs above, but when used as premed it is indicated for use prior to ketamine general anesthesia.

Pharmacology/Actions

Dexmedetomidine is the dextrorotatory enantiomer of the alpha-2 adrenergic agonist, medetomidine. The other enantiomer, levomedetomidine is thought to be pharmacologically inactive so dexmedetomidine is about two times more potent than medetomidine.

Dexmedetomidine is much more specific than xylazine for alpha$_2$ receptors versus alpha$_1$ receptors. The pharmacologic effects of dexmedetomidine include: depression of CNS (sedation, anxiolysis), analgesia, GI (decreased secretions, varying affects on intestinal muscle tone) and endocrine functions, peripheral and cardiac vasoconstriction, bradycardia, respiratory depression, diuresis, hypothermia, analgesia (somatic and visceral), muscle relaxation (but not enough for intubation), and blanched or cyanotic mucous membranes. Effects on blood pressure are variable, but dexmedetomidine can cause hypertension longer than does xylazine.

Pharmacokinetics

In dogs after IM administration, dexmedetomidine is absorbed (bioavailability 60%) and reaches peak plasma levels in about 35 minutes. Volume of distribution is 0.9 L/kg and elimination half-life is approximately 40–50 minutes. The drug is primarily metabolized in the liver via glucuronidation and N-methylation. No metabolites are active and they are eliminated primarily in the urine and to lesser extent in the feces.

In cats after IM administration, dexmedetomidine is absorbed and reaches peak plasma levels of about 17 ng/mL occur in about 15 minutes. Volume of distribution is 2.2 L/kg and elimination half-life is approximately 1 hour. Metabolites are eliminated primarily in the urine and to lesser extent in the feces.

In humans after IV administration, dexmedetomidine is rapidly distributed, undergoes almost complete biotransformation via both glucuronidation and CY-450 enzymes systems and has a terminal elimination half-life of about 2 hours. Metabolites are eliminated in the urine and feces.

Contraindications/Precautions/Warnings

The European labeling states not to use in puppies less than 6 months old or in kittens less than 5 months old; in animals with cardiovascular disorders; in animals with severe systemic disease or that are moribund; or in animals known to be hypersensitive to the active substance or any of the excipients.

Use with caution in animals with, or prone to developing, seizures. Dexmedetomidine lowered the seizure threshold in cats undergoing anesthesia with enflurane.

Adverse Effects

The adverse effects reported with medetomidine or dexmedetomidine are essentially extensions of their pharmacologic effects including bradycardia, muscle tremors, transient hypertension, occasional AV blocks, decreased respiration, hypothermia, urination, vomiting, hyperglycemia, and pain on injection (IM). Rare effects that have been reported, include: prolonged sedation, paradoxical excitation, hypersensitivity, pulmonary edema, apnea, and death from circulatory failure.

Reproductive/Nursing Safety

The drug is not recommended for use in pregnant dogs or those used for breeding purposes because safety data for use during pregnancy is insufficient; therefore use only when the benefits clearly outweigh the drug's risks. However, no teratogenic effects were observed when rats were given up to 200 mcg/kg SC from days 5–16 of gestation or when rabbits were given up 96 mcg/kg IV from days 6–18 of gestation. 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.*)

Dexmedetomidine is distributed into the milk of lactating rats; safe use during nursing has not been established.

Overdosage/Acute Toxicity

Single doses of up to 5X (IV) and 10X (IM) were tolerated in dogs, but adverse effects can occur (see above). Because of the potential of additional adverse effects occurring (heart block, PVC's, or tachycardia), treatment of medetomidine-induced bradycardia with anticholinergic agents (atropine or glycopyrrolate) is usually not recommended. Atipamezole is probably a safer choice to treat any medetomidine-induced effect.

Drug Interactions

Note: Before attempting combination therapy with dexmedetomidine, it is strongly advised to access references from veterinary anesthesiologists familiar with the use of this product.

- **ANESTHETICS, OPIATES, SEDATIVE/HYPNOTICS:** Effects may be additive; dosage reduction of one or both agents may be required

The following drug interactions have either been reported or are theoretical in humans or animals receiving medetomidine (a related compound) and may be of significance in veterinary patients:

- **ATROPINE, GLYCOPYRROLATE:** The use of atropine or glycopyrrolate to prevent or treat medetomidine-caused bradycardia is controversial as tachycardia and hypertension may result. This is more