DEXAMETHASONE
DEXAMETHASONE SODIUM PHOSPHATE
DEXAMETHASONE 21-ISONICOTINATE

Note: For more information refer to the monograph: Glucocorticoids, General Information.

Prescriber Highlights -
- Injectable, oral and 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 and as little as possible for as short an amount of time as possible
- Primary adverse effects are "cushingoid" in nature w/sustained use
- Many potential drug and lab interactions

Chemistry - 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 of is soluble in about 2 ml of water; it is slightly soluble in alcohol. Dexamethasone 21-isonicotinate occurs as a nearly odorless and tasteless, white to slight yellow, crystalline powder.

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.

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.

It is reportedly **incompatible** with: daunorubicin HCl, doxorubicin HCl, metaraminol bitartrate, and vancomycin. Compatibility is dependent upon factors such as pH, concentration, temperature and diluents used. It is suggested to consult specialized references for more specific information (*e.g., Handbook on Injectable Drugs* by Trissel; see bibliography).

Contraindications/Precautions - Because dexamethasone has negligible mineralocorticoid effect, it should generally not be used alone in the treatment of adrenal insufficiency. For more information refer to the Glucocorticoid monograph.

Systemic use of glucocorticoids are generally considered to be contraindicated in systemic fungal infections (unless used for replacement therapy in Addison's), when administered IM in patient's with idiopathic thrombocytopenia and in patient's hypersensitive to a particular compound. Use of sustained-release injectable glucocorticoids are considered to be contraindicated for chronic corticosteroid therapy of systemic diseases.

Animals who 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/Warnings - 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 symptoms of hyperadrenocorticism. When administered to young, growing animals, glucocorticoids can retard growth. 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 the drug is given. 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.

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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.

Overdosage - 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 symptoms 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 - **Amphotericin B** or potassium-depleting diuretics (**furosemide, thiazides**) when administered concomitantly with glucocorticoids may cause hypokalemia. When these drugs 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 are recommended.

Glucocorticoids may reduce **salicylate** blood levels.

Insulin requirements may increase in patients taking glucocorticoids. **Phenytoin, phenobarbital, rifampin** may increase the metabolism of glucocorticoids.

Concomitant administration of glucocorticoids and **cyclosporin** 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. Glucocorticoids may also inhibit the hepatic metabolism of **cyclophosphamide**. Dosage adjustments may be required.

Mitotane may alter the metabolism of steroids; higher than usual doses of steroids may be necessary to treat mitotane-induced adrenal insufficiency.

Patients taking 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.

Administration of **ulcerogenic drugs** (*e.g.*, **non-steroidal antiinflammatory drugs**) with glucocorticoids may increase the risk of gastrointestinal ulceration.

The effects of **hydrocortisone**, and possibly other glucocorticoids, may be potentiated by concomitant administration with **estrogens**.

In patients with myasthenia gravis, concomitant glucocorticoid and **anticholinesterase agent** (*e.g.*, pyridostigmine, neostigmine, etc.) administration may lead to profound muscle weakness. If possible, discontinue anticholinesterase medication at least 24 hours prior to corticosteroid administration.

Drug/Laboratory Interactions - 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.

Monitoring Parameters - 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 judgement should adverse effects be noted:

1) Weight, appetite, signs of edema
2) Serum and/or urine electrolytes
3) Total plasma proteins, albumin
4) Blood glucose
5) Growth and development in young animals
6) 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.

Doses -

Dogs:

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 1.0 mg/kg IV dexamethasone. Draw post-dose samples at 4 hours and 8 hours. Use 1.0 mg/kg dose if not suppressed at lower dose (0.1 mg/kg). Use 1.0 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:
(Note: Many clinicians do not recommend using this 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 toy breed dogs with hydrocephalus:

a) 0.25 mg/kg *tid - qid*; 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 2.0 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 *bid-tid* for 24 hours. Then 0.2 mg/kg SC or IV *bid-tid* for 2-3 days. Then 0.1 mg/kg IV or SC *bid-tid* for 3-5 days. (Schunk 1988a)

To reduce intracerebral pressure and edema:

a) In the palliative therapy of intracranial neoplasms: 0.25 - 2.0 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 *bid* 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 - 1.0 mg/kg SC, *bid-tid* for 24 hours, then 0.1 mg/kg SC or PO *bid* 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 *bid* 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 - 1.0 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 1/2 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 *qid* (Grauer and Hjelle 1988b)

For labeled indications (anti-inflammatory/glucocorticoid agent) for dexamethasone injection (*Azium®*):
a) 0.5 - 1 mg IV or IM; may be repeated for 3-5 days. (Package Insert; *Azium®*— Schering)

For labeled indications (anti-inflammatory/glucocorticoid agent) for dexamethasone tablets (*Azium®*):
a) 0.25 - 1.25 mg daily in single or two divided doses (Package Insert; *Azium® Tablets*— Schering)

For labeled indications (various inflammatory conditions associated with the musculoskeletal system) for dexamethasone 21-isonicotinate (*Voren®*):
a) 0.25 - 1 mg IM; may repeat for 3-5 days. (Package Insert; *Voren®*— Bio-ceutic)

Cats:

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/m^2 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 once to 3 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)

For labeled indications (anti-inflammatory agent) for dexamethasone injection (*Azium®*):
a) 0.125 - 0.5 mg IV or IM; may be repeated for 3-5 days. (Package Insert; *Azium®*— Schering)

For labeled indications (anti-inflammatory/glucocorticoid agent) for dexamethasone tablets (*Azium®*):
a) 0.125 - 0.5 mg daily in single or divided doses (Package Insert; *Azium® Tablets*— Schering)

For labeled indications (various inflammatory conditions associated with the musculoskeletal system) for dexamethasone 21-isonicotinate (*Voren®*):
a) 0.125 - 0.5 mg IM; may repeat for 3-5 days. (Package Insert; *Voren®*— Bio-ceutic)

Rabbits/Rodents/Pocket Pets:
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)