## **Regulatory Information**

Do not administer to animals intended for food. Racing Commissioners International (RCI) Classification: 3

## Betamethasone

bay-tah-meth'ah-sone

**Trade and other names:** Celestone, BetaVet, betamethasone acetate, and betamethasone benzoate

Functional classification: Corticosteroid

## Pharmacology and Mechanism of Action

Potent, long-acting corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 30 times more than those of cortisol. Anti-inflammatory effects are complex but primarily occur via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

#### **Indications and Clinical Uses**

Betamethasone is used for treatment of inflammatory and immune-mediated disease. It is used for similar indications as prednisolone and dexamethasone. The equine formulation (BetaVet) is a combination of a slow-release component (betamethasone acetate) and a rapid-acting form (betamethasone sodium phosphate) in a combination for injection intra-articularly for control of pain and inflammation associated with osteoarthritis in horses.

#### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

There are many side effects from corticosteroids, which include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal axis suppression. Adverse effects include gastrointestinal (GI) ulceration, hepatopathy, increased risk of diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and urinary tract infections. In horses, some equine clinicians have suggested that the use may increase risk of laminitis, but this has not been supported with clinical research.

#### **Contraindications and Precautions**

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, and pregnant animals. Do not inject equine product intra-articular if there are signs of infection in the joint.

#### **Drug Interactions**

No drug interactions are reported in animals. However, co-administration with other drugs may increase risk of adverse effects. For example, administration with NSAIDs may increase the risk of GI problems.

## Instructions for Use

Betamethasone is used for similar indications as dexamethasone because of similar potency and duration of effect. Topical forms of betamethasone also are available.

## **Patient Monitoring and Laboratory Tests**

Monitor complete blood count (CBC) and plasma cortisol.

## Formulations

- Betamethasone is available in 600-mcg (0.6-mg) tablets and 3-mg/mL sodium phosphate injection. (Tablets have been discontinued from some manufacturers and are difficult to obtain.)
- Equine formulation (BetaVet) contains betamethasone sodium phosphate (rapid acting) and betamethasone acetate (slow release) in a suspension for intra-articular use at a concentration of 6 mg/mL (3.15 mg in betamethasone sodium phosphate and 2.85 mg in betamethasone acetate).

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. After opening the equine product (BetaVet), use once and discard vial after use.

## **Small Animal Dosage**

## Dogs and Cats

(Oral formulations may not be available.)

- Anti-inflammatory effects: 0.1–0.2 mg/kg q12–24h PO.
- Immunosuppressive effects: 0.2–0.5 mg/kg q12–24h PO.

## Large Animal Dosage

- 0.05–0.1 mg/kg q24h IM or PO.
- Intra-articular injection. The equine intra-articular product can be injected at a dose of 1.5 mL per joint (9 mg).

## **Regulatory Information**

No withdrawal times are established for animals intended for food (extralabel use). RCI Classification: 4

## **Bethanechol Chloride**

beh-than'eh-kole klor'ide

Trade and other names: Urecholine

Functional classification: Cholinergie

## Pharmacology and Mechanism of Action

Muscarinic, cholinergic agonist. Parasympathomimetic. Bethanechol stimulates gastric and intestinal motility. It also stimulates contraction of the urinary bladder via muscarinic receptor activation. Bethanechol, like other carbamoyl esters, resists hydrolysis by acetylcholinesterase to produce a more sustained response. The onset of action is usually 10 minutes after injection and 30–60 minutes after oral administration. Duration of effect is 4–6 hours. Calves

 30 mcg/kg IV or detomidine oral mucosal gel (equine formulation): 80 mcg/kg.

#### **Regulatory Information**

Cattle withdrawal times (extralabel): 3 days meat; 72 hours milk. For extralabel uses and doses, contact FARAD at www.FARAD.org. RCI Classification: 3

## Dexamethasone

deks-ah-meth'ah-sone

**Trade and other names:** Azium solution in polyethylene glycol, DexaJect, Dexavet, Decadron, Dexasone, Voren suspension, and generic brands

Functional classification: Corticosteroid

## Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects of dexamethasone are approximately 30 times more potent than cortisol and 6–7 times more potent than prednisolone. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. The most important use is for treatment of inflammatory and immune-mediated disease. This dexamethasone solution differs from dexamethasone sodium phosphate in that the sodium phosphate form is water soluble and appropriate for IV administration. See the next section for more information about dexamethasone sodium phosphate. Dexamethasone solution is in a polyethylene glycol vehicle that should not be administered rapidly IV.

Dexamethasone-21-isonicotinate is a suspension registered for IM use (usually for horses). After an injection of 10 mg (total dose) to horses, the half-life was 2.5–5 hours, and the volume of distribution (VDss) was 1.7 L/kg. Oral administration of the same dose had a half-life of 4.3 hours and bioavailability (F) of 61%, with a peak concentration at 1.3 hours. In horses, oral absorption is higher in unfed horses, and oral absorption from powder is higher than with solution. The suspension (dexamethasone-21-isonicotinate) has a slow release and produces a 39-hour half-life in horses and suppresses cortisol for 140 hours.

## Indications and Clinical Uses

Dexamethasone is used for treatment of inflammatory and immune-mediated disease. The use of dexamethasone at high doses for treatment of shock is controversial. Most recent evidence does not support administration of dexamethasone for this use unless there is adrenal deficiency. Dexamethasone is often used short term in small animals as an injection (sodium-phosphate form) when oral treatment with prednisone is not possible. Dexamethasone is also used as a diagnostic test of adrenal function. Large animal uses include induction of parturition (cattle) and treatment of inflammatory conditions. In cattle, corticosteroids also have been used in the treatment of ketosis. In horses, dexamethasone has been used to treat equine asthma syndrome, with bronchoconstriction caused by recurrent airway obstruction (RAO).

## **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Side effects from corticosteroids are many and include polyphagia, polydipsia and polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, increased risk of diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include infections from *Demodex* spp., toxoplasmosis, fungal infections, and urinary tract infections (UTIs). Highdose glucocorticoids in animals with neurologic disease can lead to excitotoxic cell death and oxidative injury via increased excitatory amino acids. In horses, dexamethasone adverse effects have included risk of laminitis, although this effect is controversial and not supported by strong evidence.

#### **Contraindications and Precautions**

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in animals with diabetes or renal failure and in pregnant animals. IV injections should be done slowly because formulations contain polyethylene glycol, which can cause reactions from rapid IV injection (hemolysis, hypotension, and collapse). Do not administer dexamethasone-21-isonicotinate IV (IM use only).

#### **Drug Interactions**

Administration of corticosteroids with NSAIDs increases the risk of GI injury. The pH of the solution is 7–8.5. Do not mix with acidifying solutions, or it may not be compatible. Otherwise, it is compatible with most IV fluid solutions.

## Instructions for Use

For IV administration, the dexamethasone sodium phosphate solution is preferred (Dex S P) because of better water solubility for IV use. (See Dexamethasone Sodium Phosphate.)-Dosing schedules are based on the condition treated. Anti-inflammatory effects occur at doses of 0.1–0.2 mg/kg, and immunosuppressive effects occur at 0.2–0.5 mg/kg.

Dexamethasone is used to test for hyperadrenocorticism. For the low-dose dexamethasone suppression test, administer to dogs, 0.01 mg/kg (or 0.015 mg/kg in some references) IV, and to cats, 0.1 mg/kg IV; collect samples at 0, 4, and 8 hours. For high-dose dexamethasone suppression test: administer to dogs, 0.1 mg/kg (or 1.0 mg/kg in some references), and to cats, 1.0 mg/kg.

## **Patient Monitoring and Laboratory Tests**

For the low- and high-dose dexamethasone suppression tests, administer either 0.01 or 0.1 mg/kg and collect cortisol samples at 0, 4, and 8 hours after administration. The normal cortisol concentration after suppression test should be less than 30-40 nmol/L (1.1–1.3 mcg/dL). For the dexamethasone suppression test for horses, administer 0.04 mg/kg IM and collect postcortisol sample 24 hours later. Normal suppression in horses is less than 1 mcg/dL.

## **Formulations**

• Dexamethasone is available in a 2-mg/mL solution, which contains 500 mg of polyethylene glycol; 0.25-, 0.5-, 0.75-, 1-, 1.5-, 2-, 4-, and 6-mg tablets; 0.1- and 1-mg/mL oral solution; and 10 mg per 15 g powder. Dexamethasone-21- isonicotinate slow-release suspension in an aqueous vehicle is 1 mg/mL.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Dexamethasone formulated in various oral mixtures to enhance flavoring was stable for 26 weeks at room temperature or refrigerated. Dexamethasone sodium phosphate is freely soluble in water, but dexamethasone solution (in polyethylene glycol) is practically insoluble in water.

## Small Animal Dosage

## Dogs and Cats

- Anti-inflammatory: 0.07–0.15 mg/kg q12–24h IV, IM, or PO.
- Oral dosage (cats): 0.1–0.2 mg/kg q24h PO, added to food. After the initial dose, lower to a maintenance dosage of 0.05 mg/kg q48–72h PO.
- Immunosuppressive: 0.125–0.25 mg/kg q24h IV, IM, or PO for initial treatment.
- Pulse dose: 0.5 mg/kg PO for 4 consecutive days; then repeated every 28 days.
- $\bullet\,$  Low-dose dexame thasone suppression test: 0.01 mg/kg IV (dog) and 0.1 mg/kg IV (cat).
- $\bullet\,$  High-dose dexame thasone suppression test: 0.1 mg/kg IV (dog) and 1.0 mg/kg IV (cat).
- Dexamethasone-21-isonicotinate: 0.03–0.05 mg/kg IM.

## Large Animal Dosage

## Cattle and Horses

- 0.04–0.15 mg/kg per day IV or IM. Some product labeling lists a total dose of 5–20 mg/animal, which corresponds to 0.01-0.04 mg/kg/day. However, for some conditions, higher doses may be needed.
- Horses, treatment of equine asthma syndrome (airway disease caused by RAO): 0.05–0.1 mg/kg IV or IM q24h or 0.165 mg/kg PO q24h, usually for 2–3 days, but oral treatment has been continued for 7 days; then tapered to half the dose for another 7 days.
- Induction of parturition (cattle): 0.05 mg/kg (25 mg/animal) as a single dose during the last week or 2 weeks of pregnancy. A dose of prostaglandin (PG) F<sub>2</sub> alpha may be administered concurrently (0.5 mg/animal).
- Dexamethasone-21-isonicotinate: 0.01–0.04 mg/kg IM.

## Sheep

• Induction of parturition: 0.15 mg/kg/day IM for 1–5 days during the last week of gestation.

## **Regulatory Information**

Dexamethasone is approved for use in cattle, but withdrawal times are not established. Although withdrawal times are not listed on the label, at least 96 hours should be used for milk and 4–8 days for meat. Allow at least 3 weeks to eliminate residues from the kidneys and liver and 6 weeks to deplete the drug from the IM injection site. For other extralabel uses, contact FARAD at www.FARAD.org. RCI Classification: 4

## **Dexamethasone Sodium Phosphate**

**Trade and other names:** Sodium phosphate: DexaJect SP, Dexavet, and Dexasone; Decadron and generic brand tablets

Functional classification: Corticosteroid

## **Small Animal Dosage**

## Dogs

- Antitussive dose: 0.5 mg/kg q8 h PO. Increase the dose if needed for tracheal collapse in dogs but not above the dose of 1.5 mg/kg.
- Analgesic dose: 0.5 mg/kg q8-12 h PO. (Analgesic properties have not been established in dogs.)

## Cats

• No dose has been established. Oral doses may be effective in cats, but caution should be used because many formulations contain acetaminophen.

## Large Animal Dosage

• No large animal doses have been reported.

## **Regulatory Information**

Hydrocodone is a Schedule II drug controlled by the Drug Enforcement Administration (DEA).

Hydrocodone is not recommended for food-producing animals. If administered to a food animal, consult FARAD for extralabel use withdrawal interval estimates (www.FARAD.org).

RCI Classification: 1. Do not administer to racing horses.

# Hydrocortisone hye-droe-kor'tih-sone

Trade and other names: Hydrocortisone, Cortef and generic brands, hydrocortisone sodium succinate, Solu-Cortef

Functional classification: Corticosteroid

## Pharmacology and Mechanism of Action

Hydrocortisone is a glucocorticoid anti-inflammatory and adrenal replacement drug. Hydrocortisone has weaker anti-inflammatory effects and greater mineralocorticoid effects compared with prednisolone or dexamethasone. Hydrocortisone has properties that most closely resemble natural cortisol in the body. It is about 1/5 the potency of prednisolone and 1/25 the potency of dexamethasone. The most common use is to mimic the effects of cortisol when used in patients with hypoadrenocorticism (patients with adrenal insufficiency). Anti-inflammatory effects are complex but are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

## Indications and Clinical Uses

Hydrocortisone is used most often for adrenal corticosteroid replacement treatment in patients with adrenal insufficiency. It is less often used for its anti-inflammatory effects and not used as commonly as other corticosteroids such as prednisolone or dexamethasone except when hormone replacement to mimic the effects of cortisol is needed. Hydrocortisone sodium succinate is a rapid-acting injectable product that can be used when a prompt response is needed.

## **Precautionary Information**

#### **Adverse Reactions and Side Effects**

At the doses used for replacement therapy, serious adverse effects are uncommon. Other side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal axis suppression. Adverse effects include gastrointestinal (GI) ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and urinary tract infections. In horses, additional adverse effects may include risk of laminitis, but this is poorly documented in horses unless they have predisposing factors.

#### **Contraindications and Precautions**

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals.

#### **Drug Interactions**

Glucocorticoids are often synergistic with other anti-inflammatory and immunosuppressive drugs. Administration of corticosteroids with nonsteroidal anti-inflammatory drugs increases the risk of GI injury.

## Instructions for Use

Because the most common use is for adrenal replacement therapy in adrenal insufficiency, the doses administered are intended to mimic the natural release of cortisol in the body. Typically for replacement therapy (e.g., in animals with hypoadrenocorticism) dosages start at 1 mg/kg/day.

#### Patient Monitoring and Laboratory Tests

Monitor electrolytes (sodium and potassium) in animals being treated for hypoadrenocorticism. Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

## Formulations

• Hydrocortisone is available in 5-, 10-, and 20-mg tablets, and hydrocortisone sodium succinate is available in various size vials for injection.

#### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Hydrocortisone is slightly soluble in water and is soluble in alcohol. Degradation occurs at a high pH above 7–9. Compounded suspensions have been stable for 30 days. Most compounded topical ointments and lotions are stable for 30 days.

#### Small Animal Dosage

#### Dogs and Cats

#### Hydrocortisone

- Replacement therapy: 1–2 mg/kg q12h PO.
- Anti-inflammatory: 2.5–5 mg/kg q12h PO.

#### 438 Hydromorphone

#### Hydrocortisone Sodium Succinate

- Hypoadrenocorticism (adrenal crisis): 0.625 mg/kg/h, IV CRI.
- Shock: (not a recommended use) 50–150 mg/kg IV for two doses 8 hours apart.
- Anti-inflammatory: 5 mg/kg q12h IV.

## Large Animal Dosage

## Horses

• Hydrocortisone sodium succinate: 5 mg/kg q12h IV.

#### Foals

• Replacement therapy for critical illness: 1-3 mg/kg/day IV.

## **Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org. RCI Classification: 4

## **Hydromorphone**

hye-droe-mor/fone

Trade and other names: Dilaudid, Hydrostat, and generic brands

Functional classification: Analgesic, opiate

## Pharmacology and Mechanism of Action

Hydromorphone is an opioid agonist, analgesic. Like other opiates, it binds to muopiate and kappa-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (e.g., substance P). Opiates also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to mu-receptor effects in the brain. Hydromorphone has similar qualitative properties as morphine but is six or seven times more potent than morphine. Other opiates used in animals include morphine, codeine, oxymorphone, meperidine, and fentanyl.

*Pharmacokinetics*: In dogs, the half-life after IV administration was 70–80 minutes. When PO hydrocodone is administered to animals, it is partially metabolized to hydromorphone (hydrocodone discussed earlier).

## **Indications and Clinical Uses**

Hydromorphone is used in animals for analgesia and sedation and as an adjunct for anesthesia. In dogs and cats, it is used as a single agent or in combination with other agents. Hydromorphone is similar in action to morphine; however, it is more potent than morphine (6–7×) and should be used at lower doses. Hydromorphone is approximately half as potent as oxymorphone. Studies in dogs indicate that hydromorphone at equivalent doses is equal to oxymorphone for producing sedation in dogs. In cats, duration of effect (0.1 mg/kg) has been 6–7.5 hours despite a relatively short plasma half life of 1–1.5 hours.

#### 598 Methylprednisolone

morphine on GI motility. However, at the dose studied (0.75 mg/kg), it did not fully antagonize the effects of morphine.

Precautionary Information Adverse Reactions and Side Effects

Adverse effects are only reported for people and include abdominal pain and diarrhea. Although it is an opiate antagonist, it has not triggered breakthrough pain.

Contraindications and Precautions

Do not use if there is intestinal obstruction.

**Drug Interactions** 

No drug interactions have been reported for animals.

**Instructions for Use** 

The use in animals is primarily experimental and has been limited in clinical practice.

Patient Monitoring and Laboratory Tests No specific monitoring is necessary.

**Formulations** 

Methylnaltrexone is available by injection only. It is available in 12 mg vials (0.6 mL), equivalent to 20 mg/mL in each vial.

Stability and Storage Store in a tightly sealed container, protected from light, and at room temperature.

Small Animal Dosage Dogs and Cats • 0.15 mg/kg SQ injection once per 24 or 48 hours.

Large Animal Dosage Horses

0.75 mg/kg IV q12h every 4 days.

**Regulatory Information** 

No withdrawal information is available for food-producing animals.

## Methylprednisolone

meth-il-pred-niss'oh-lone

**Trade and other names:** Methylprednisolone: Medrol; methylprednisolone acetate: Depo-Medrol; and methylprednisolone sodium succinate: Solu-Medrol

Functional classification: Corticosteroid

## Pharmacology and Mechanism of Action

Methylprednisolone is a glucocorticoid anti-inflammatory drug. It is administered by the oral route, injection, and local delivery. The anti-inflammatory effects are complex, but they operate primarily via inhibition of inflammatory cells and suppression of inflammatory mediators. Compared with prednisolone, methylprednisolone is 1.25 times more potent.

#### **Indications and Clinical Uses**

Methylprednisolone acetate is a long-acting depot formulation of methylprednisolone. It is slowly absorbed from the IM injection site producing glucocorticoid effects for 3–4 weeks in some animals. Methylprednisolone acetate is used for intralesional therapy, intraarticular administration for joint disease, and for treating other inflammatory conditions. Methylprednisolone sodium succinate is a water-soluble formulation intended for acute therapy when high IV doses are needed for rapid effect. It has been administered IV for treatment of shock and trauma of the CNS. Methylprednisolone oral tablets are used for treatment of conditions in animals that require short- to long-term therapy with an intermediate-acting corticosteroid. The indications for methylprednisolone tablets are similar to the use of prednisolone or prednisone tablets except that methylprednisolone is slightly more potent. Conditions treated include dermatitis, immune-mediated diseases, intestinal diseases, and neurologic and musculoskeletal diseases. Although high doses have been used to treat spinal cord trauma, this use has questionable benefit in animals. In large animals, methylprednisolone acetate is used for treatment of inflammatory conditions of the musculoskeletal system. Intra-articular administration is common in horses.

## **Precautionary Information**

## **Adverse Reactions and Side Effects**

Side effects from corticosteroids are many and include polyphagia, polydipsia and polyuria, and hypothalamic-pituitary-adrenal axis suppression. However, the manufacturer suggests that methylprednisolone causes less polyuria and polydipsia than prednisolone. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Dogs that receive high doses of methylprednisolone succinate (e.g., 30 mg/kg) have a high risk of GI bleeding. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs.

In cats, injections of methylprednisolone may activate latent feline herpes virus infections in some cats. In cats, there is a concern that corticosteroids such as methylprednisolone can exacerbate congestive heart failure (CHF) through volume expansion and fluid shifts secondary to steroid-induced hyperglycemia. This has occurred in susceptible cats after injections of methylprednisolone acetate. In cats, methylprednisolone acetate injections have caused injection-site alopecia.

In horses, additional adverse effects may include risk of laminitis (although a direct link to induction of laminitis is controversial).

#### **Contraindications and Precautions**

Use cautiously in patients prone to GI ulcers and infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with kidney disease, and pregnant animals. Use cautiously in cats because of volume expansion, especially cats at risk of CHF.

#### **Drug Interactions**

Like other corticosteroids, if methylprednisolone is administered with NSAIDs, there is increased risk of GI ulcers.

## **Instructions for Use**

The list of doses below are initial doses. If the patient responds and is stabilized, the dose may be tapered to the lowest dose possible (as low as 0.25 mg/kg/day) and possibly administered every other day.

### 600 Methylprednisolone

Use of methylprednisolone is similar to other corticosteroids, such as prednisone or prednisolone. Dose adjustment should be made to account for difference in potency if interchanged with prednisone, dexamethasone, or triamcinolone acetonide. Use of methylprednisolone acetate should be evaluated carefully because one injection will cause glucocorticoid effects that persist for several days to weeks. There are no published studies that have evaluated the use of methylprednisolone sodium succinate in animals, but the use has been extrapolated from human medicine.

## **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and kidney function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone stimulation test to monitor adrenal function. Monitor cats for diabetes and heart disease when treated with methylprednisolone acetate.

## **Formulations**

- Methylprednisolone is available in 1-, 2-, 4-, 8-, 18-, and 32-mg tablets.
- Methylprednisolone acetate is available in 20- and 40-mg/mL suspension for injection.
- Methylprednisolone sodium succinate is available in 1- and 2-g and 125- and 500mg vials for injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Methylprednisolone is insoluble in water and slightly soluble in ethanol. Methylprednisolone acetate is slightly soluble in water. Methylprednisolone sodium succinate is highly soluble in water. When methylprednisolone sodium succinate is reconstituted, it should be used within 48 hours if kept at room temperature. Decomposition occurs with longer storage. It may be frozen at  $-20^{\circ}$ C for 4 weeks with no loss of potency.

## **Small Animal Dosage**

## Dogs

- Methylprednisolone oral tablets: 0.25–0.5 mg/kg q12–24h PO, with the dose dependent on the severity of the disease. The label dosage is 0.22–0.44 mg/kg q12–24h PO. After starting the initial dose, slowly taper the dose and frequency to the lowest dose possible that will control the disease condition. Long-term maintenance doses are in the range of 0.3–0.5 mg/kg every other day, PO.
- Methylprednisolone acetate: 1 mg/kg (or 20–40 mg/dog) IM every 1–3 weeks.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2–6 hours IV.
- Replacement therapy for adrenal insufficiency: 0.2 mg/kg/day.

## Cats

- Methylprednisolone oral tablets: 0.25–0.5 mg/kg q12–24h PO, with the dosage dependent on the severity of the disease. The label dosage is 0.22–0.44 mg/kg q12–24h PO. After starting the initial dose, slowly taper the dose and frequency to the lowest dose possible that will control the disease condition.
- Methylprednisolone acetate: 10-20 mg/cat IM every 1-3 weeks.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2–6 hours IV.

## Large Animal Dosage

## Horses

- 200 mg as a single total dose injected intramuscularly.
- Intra-articular dose: 40–240 mg total dose, with the average dose of 120 mg injected in the joint space using sterile technique.

## **Regulatory Information**

In horses, 200 mg per joint was detected in horses for 18 days; 100 mg per joint was detected for 7 days. For food animals, withdrawal times are not established. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org. RCI Classification: 4

## **Methyltestosterone**

meth-ill-tess-toss'teh-rone

Trade and other names: Android and generic brands

Functional classification: Hormone, anabolic agent

#### Pharmacology and Mechanism of Action

Methyltestosterone is a form of testosterone used as an anabolic androgenic agent. Injections of methyltestosterone mimic the effects of testosterone and are used as a replacement for testosterone or for use in debilitated animals that require an anabolic agent.

## Indications and Clinical Uses

Methyltestosterone is used for anabolic actions or testosterone hormone replacement therapy (androgenic deficiency). Testosterone has been used to stimulate erythropoiesis. Other similar agents used include testosterone cypionate and testosterone propionate.

#### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects are caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations than with non-methylated forms. Therefore, monitor bilirubin and hepatic enzymes for evidence of liver reactions.

#### **Contraindications and Precautions**

Do not administer to pregnant animals.

#### **Drug Interactions**

No drug interactions have been reported for animals.

#### Instructions for Use

Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. The clinical use is based primarily on experimental evidence or experiences in people.

#### Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes and clinical signs for evidence of cholestasis and hepatotoxicity during treatment.

#### **Formulations**

Methyltestosterone is available in 10- and 25-mg tablets.

## **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes, especially ALP, because of enzyme induction, without inducing liver pathology. Prednisolone can increase WBC count and decrease lymphocyte count. It can increase serum albumin, glucose, triglycerides, and cholesterol. Corticosteroid administration may decrease conversion of thyroid hormones to its active form. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

### **Formulations**

 Prednisolone sodium succinate is available in 100 and 500 mg vials for injection (10, 20, and 50 mg/mL). For some indications, methylprednisolone sodium succinate (Solu Medrol) has been substituted.

#### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisolone sodium succinate should be used immediately after reconstitution. Do not freeze. If solution becomes cloudy, do not administer intravenously.

#### **Small Animal Dosage**

#### **Dogs and Cats**

- Shock (effectiveness of this use is controversial): 15-30 mg/kg IV (repeat in 4-6 hours).
- CNS trauma: 15-30 mg/kg IV, taper to 1-2 mg/kg q12h.
- Anti-inflammatory: 1 mg/kg/day IV.
- Replacement therapy for adrenal insufficiency: 0.25-0.5 mg/kg/day IV.
- Intermittent treatment (pulse therapy) of pemphigus foliaceus: 10 mg/kg IV.

#### Large Animal Dosage

#### Horses

- 0.5 1 mg/kg q12 24h IM or IV. IV dose should be given slowly over 30 60 seconds.
- Treatment of shock (although efficacy for treating shock has not been established): 15–30 mg/kg IV; repeat dose in 4–6 hours.

#### **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

RCI Classification: 4

## Prednisone

pred'nih-sone

Trade and other names: Deltasone, Meticorten, and generic brands Functional classification: Corticosteroid

## Pharmacology and Mechanism of Action

Prednisone is the inactive form of prednisolone. After administration in most animals (except horses and cats), prednisone is converted to prednisolone, and the effects listed for prednisolone are expected.

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#### 772 Prednisone

Prednisone is a glucocorticoid anti-inflammatory drug. The effect of prednisone is attributed to prednisolone. Anti-inflammatory effects are complex, but via binding to cellular glucocorticoid receptors, prednisolone acts to inhibit inflammatory cells and suppresses expression of inflammatory mediators. Prednisolone is approximately four times more potent than cortisol but only one seventh as potent as dexamethasone. Prednisone appears to be well absorbed and converted to active drug in dogs. However, in horses and cats, administration of prednisone results in low systemic levels of the active drug prednisolone, either because of poor absorption of prednisone or because of a deficiency in converting prednisone into prednisolone.

### Indications and Clinical Uses

Prednisone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated diseases. In cats, prednisone may produce therapeutic failures, and prednisolone (active drug) is preferred. There is evidence of poor conversion of prednisone to prednisolone or poor absorption of prednisone in cats and horses. Prednisolone or another active drug (e.g., triamcinolone, dexamethasone) should be used instead for these animals. There are several large animal doses cited (similar to prednisolone); however, because of poor activity in horses, the use is discouraged.

#### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

There are many side effects from corticosteroids that include polyphagia, polydipsia and polyuria, behavior changes, and HPA axis suppression. Adverse effects include GI ulceration, diarrhea hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone (but not free  $T_4$ ), decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs.

In dogs, prednisolone administration increased vascular resistance, systolic blood pressure, and increase cardiac afterload. This could potentially exacerbate CHF in some dogs. Thus, in dogs with heart disease, prednisolone should be used carefully.

#### **Contraindications and Precautions**

Use corticosteroids cautiously in patients with a risk of GI ulcers or infections and in animals in which growing or healing is necessary. Use prednisone cautiously in patients with renal disease because it may cause azotemia. Use prednisone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents.

#### **Drug Interactions**

Administration of corticosteroids with NSAIDs increases the risk of GI injury. Corticosteroids may inhibit conversion of  $T_4$  thyroid hormone to the active form  $T_3$ . However, in dogs, the concentration of total  $T_4$ , but not free  $T_4$ , is decreased. Therefore, the effect on thyroid status in a canine patient is expected to be minimal.

## Instructions for Use

Prednisolone and prednisone can be used interchangeably in dogs. However, cats and horses may have problems converting prednisone to the active prednisolone or problems with oral absorption of prednisone, and prednisolone should be used instead. (Alternatively, methylprednisolone or triamcinolone can be used.) As for prednisolone, the doses vary across a broad range based on severity of the underlying condition. Consult the dosing section for the range of doses administered for each condition.

## **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes, especially ALP, without inducing liver pathology. Corticosteroid administration may decrease conversion of thyroid hormones to active form. However, in dogs receiving anti-inflammatory doses of prednisone, total T<sub>4</sub> concentrations, but not freeT<sub>4</sub>, may be decreased.

## **Formulations**

- Prednisone oral forms: 1-, 2.5-, 5-, 10-, 20-, 25-, and 50-mg tablets; 1-mg/mL syrup (Liquid Pred in 5% alcohol); and 1-mg/mL oral solution (in 5% alcohol)
- Prednisone for injection: 10- and 40-mg/mL prednisone suspension for injection (Meticorten; availability has been limited).

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Prednisone is slightly soluble in water, and it is soluble in ethanol. Prednisone has been prepared by first dissolving in ethanol and then mixing with syrups and flavorings. No loss occurred, but crystallization is common in aqueous vehicles. Prednisone tablets have been crushed and mixed with syrups and other flavorings, stored for 60 days, and found to produce equal bioavailability as tablets in people.

## **Small Animal Dosage**

#### Dogs

- Anti-inflammatory: 0.5–1 mg/kg, per day, which may be divided into twice-daily treatments, IM, or PO initially; then taper to q48h at a dose of 0.3–0.5 mg/kg.
- Immunosuppressive: 2.2–6.6 mg/kg/day IV, IM, or PO initially; then taper to 2–4 mg/kg q48h. Initial doses rarely need to exceed 4 mg/kg per day.
- Replacement therapy for adrenal insufficiency: 0.2–0.3 mg/kg/day PO.
- Neurologic disease (steroid responsive): Start with 2 mg/kg q12h PO for 2 days followed by gradual tapering to 1 mg/kg, then 0.5 mg/kg, and eventually to 0.5 mg/kg every other day.
- Cancer therapy (e.g., COAP protocol): 40 mg/m<sup>2</sup> q24h for 7 days; then 20 mg/m<sup>2</sup> every other day PO.

## Cats

• Not recommended for cats because of an inability to form active metabolite. However, if use is attempted, higher doses than used in dogs are needed.

## Large Animal Dosage

## Horses

• Prednisone suspension (Meticorten) (label dosage): 100–400 mg per horse (0.22–0.88 mg/kg) as a single dose IM to be repeated every 3–4 days. No oral doses are listed for horses because of an inability of oral treatment to produce active prednisolone concentrations.

## **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org. RCI Classification: 4

q24h, depending on the use. Alternatively, to avoid breaking tablets, give 25 or 50 mg per dog (depending on the dog's size) once daily and increase gradually to a maximum of 300 mg per dose or 900 mg per dog per day.

#### Cats

 50–100 mg per cat PO (peak effect occurs in 2–2.5 hours) as needed to control anxiety; 50 mg per cat is usually sufficient for most cats. Time to peak sedation in cats occurs in approximately 2 hours.

## Large Animal Dosage

 Trazodone has been studied in horses, but no safe and effective dose has been established.

#### **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org.

## Triamcinolone Acetonide, Triamcinolone Hexacetonide, Triamcinolone Diacetate

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**Trade and other names:** Vetalog, TriamTabs, Aristocort, Kenalog (human injection), and generic brands

#### Functional classification: Corticosteroid

#### Pharmacology and Mechanism of Action

Triamcinolone acetonide is a glucocorticoid anti-inflammatory drug. Antiinflammatory effects are complex, but they are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Some older references indicate that triamcinolone (not triamcinolone acetonide) has potency that is approximately equal to methylprednisolone (about 5 times cortisol and 1.25 times prednisolone). However, triamcinolone acetonide, has a different structure than triamcinolone, and is much more potent. This potency is 6–7 times that of prednisolone and slightly more potent than dexamethasone. Most veterinary dermatologists have observed that triamcinolone acetonide is approximately 6–10 times more potent than prednisolone. Thus, the oral doses listed reflect this higher potency.

*Pharmacokinetics*: The pharmacokinetics have not been well studied in small animals. After IV administration (not a recommended route), the half-life was 6 hours, the intra-articular half-life was 24 hours, and the half-life from IM administration was 150 hours. The long IM half-life was due to a prolonged absorption phase. The IM injection suppressed cortisol for 15 days.

## **Indications and Clinical Uses**

Triamcinolone acetonide, like other corticosteroids, is used to treat inflammatory and immune-mediated diseases in animals. It is used for similar purposes as prednisolone, except with higher potency. It is an acceptable substitute for prednisolone in cats.

Triamcinolone acetonide suspension is also used for intralesional and intraarticular injections to produce local anti-inflammatory effects. When injected IM, the suspension is absorbed slowly. Therefore, the IM injection may have a duration

# of activity lasting 2–4 weeks. After intra-articular injection, the duration may be maintained for several weeks.

In addition to joint infections, other large animal uses include treatment of inflammatory and immune-mediated conditions and for RAO, formerly called *chronic obstructive pulmonary disease*, in horses associated with equine asthma syndrome.

## **Precautionary Information**

## **Adverse Reactions and Side Effects**

Side effects from corticosteroids are many and include polyphagia, polydipsia and polyuria, and hypothalamic–pituitary–adrenal axis suppression. Injections of triamcinolone acetonide can have long-lasting effects. In people, injections can produce adrenal suppression for 30 days.

Other adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, impaired wound healing, and immunosuppression. When triamcinolone acetonide is used for ocular injections, there is some concern that granulomas may occur at the injection site. When administered to horses at a dose of 0.05 mg/kg IM, it induces hyperglycemia for 3 days, but this does not lead to laminitis. Although adverse effects typically include increased risk of laminitis in horses, evidence for this effect has been controversial and not supported by well-controlled studies.

#### **Contraindications and Precautions**

Do not administer injectable suspension IV. The injectable product is intended for IM, intra-articular, or intralesional injection. Use cautiously in patients prone to ulcers or infection and in animals in which wound healing is necessary. Do not use the ocular form in animals with corneal ulcers. Use cautiously in animals with diabetes or renal failure and in pregnant animals. Because of the high potency (equal to or slightly greater potency than dexamethasone), high doses should be avoided.

## **Drug Interactions**

Use cautiously in conjunction with NSAIDs because it may potentiate the GI adverse effects.

## Instructions for Use

Triamcinolone acetonide, like other corticosteroids such as prednisolone, is administered in a variety of doses, depending on the severity of the condition being treated. The injectable product is a suspension. Shake well before using. Note that cats may require higher doses than dogs.

### **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

## Formulations

- Vetalog (veterinary preparation of triamcinolone acetonide) is available in 0.5- and 1.5-mg tablets.
- Human preparations of triamcinolone acetonide are available in 1-, 2-, 4-, 8-, and 16-mg tablets, but many tablet sizes have been discontinued. Human tablets of 4 mg (scored tablet) are usually available.

- Triamcinolone hexacetonide (Canadian product) is available in a 5- and 20-mg/mL suspension.
- Triamcinolone diacetate is available in a 25-mg/mL suspension.
- Triamcinolone acetonide for injection is available in 10- or 40-mg/mL suspension (human form) or 2- and 6-mg/mL suspension (veterinary form).

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Avoid freezing of injectable suspension. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

- Dogs: For anti-inflammatory treatment, start with 0.1–0.2 mg/kg per day PO; then gradually taper to 0.1 mg/kg every other day. Eventually, some conditions can be controlled with 0.03–0.055 mg/kg q48h PO. (The manufacturer recommends dosages of 0.11–0.22 mg/kg/day.)
- Cats: For anti-inflammatory treatment, start with 0.2 mg/kg per day PO. Gradually taper to a dosage of 0.1 mg/kg (0.5 mg per cat [one tablet] is a common dose) every other day. Some cats can be controlled with low dosages of 0.05 mg/kg q48h.
- Immune-mediated disease (dogs and cats): triamcinolone tablets at doses of 0.2–0.6 mg/kg/day, with maintenance doses of 0.1–0.2 mg/kg q48h PO.
- Triamcinolone acetonide: 0.1–0.2 mg/kg IM or SQ; repeat in 7–10 days.
- Intralesional: 1.2–1.8 mg or 1 mg for every centimeter diameter of tumor every 2 weeks or longer.
- Intra-articular: 5–15 mg per joint for large joints; 2.5–5 mg for small joints. Injections in tendon sheaths are in the range of 2.5–5 mg.

## Large Animal Dosage

## Horses

- 12–20 mg per horse IM. The maximum recommended dose is 0.05 mg/kg IM.
- Triamcinolone acetonide suspension: 0.022–0.044 mg/kg as a single dose IM.
- RAO: 0.09 mg/kg as a single dose IM.
- Intra-articular: 6–18 mg as a total dose per joint (usually 9–12 mg). Repeat in 4–13 days if necessary.

## Cattle

• Triamcinolone acetonide is not approved in cattle, and there are no established doses. If triamcinolone acetonide suspension is injected in cattle, the same dose regimens as used in horses can be used, and extralabel withdrawal times should be followed.

## **Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at www.FARAD.org. RCI Classification: 4

## **Triamterene**

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Trade and other names: Dyrenium

Functional classification: Diuretic