CORTICOSTEROIDS—GLUCOCORTICOID EFFECTS (Veterinary—Systemic)

This monograph contains information on the following:

Dexamethasone; Flumethasone; Hydrocortisone; Isolupredone;
Methylprednisolone; Prednisolone; Prednisone; Triamcinolone.

Some commonly used brand names are:

For veterinary-labeled products—

Cortalone
[Triamcinolone] [Prednisolone]
A-methaPred
[Cortef]
Methysone 40
[Dexemethasone]
Dexamethasone 5
[Rafter Dex]
Dexone
[Solu-Delta-Cortef]
[Dexamethasone]
Dextrum [Dexamethasone]
[Triamcinolone]
Dexone [Dexamethasone]
Unimed
[Unime-Dex]
Flucort [Flumethasone]
[Hydrocortisone]
Medrol
[Methylprednisolone]
Dexone
[Dexamethasone]
[Solu-Medrol]
Methylprednisolone

For human-labeled products—

A-methaPred
[Methylprednisolone]
Cortef [Hydrocortisone]
Decadron
[Hydrocortisone]
Dexone
[Dexamethasone]
[Solu-Medrol]
[Methylprednisolone]

Note: For a listing of dosage forms and brand names by country availability, see the Dosage Forms section(s).

Category:

Abortifacient—Dexamethasone.
Anti-inflammatory agent (steroidal)—Dexamethasone;
Flumethasone; Hydrocortisone; Isolupredone;
Methylprednisolone; Prednisolone; Prednisone;
Triamcinolone.
Diagnostic aid (hyperadrenocorticism)—Dexamethasone.
Glucocorticoid agent—Dexamethasone; Flumethasone;
Isolupredone; Prednisolone.
Immunosuppressant—Prednisolone; Prednisone.
Parturifacient—Dexamethasone; Flumethasone.

Indications

Note: The text between "US" and "E" describes uses that are not included in U.S. product labeling. Text between "US,CA" and "E" describes uses that are not included in Canadian product labeling. The "US" or "US,CA" designation can signify a lack of product availability in the country indicated. See the Dosage Forms section of this monograph to confirm availability.

General considerations

Glucocorticoids potentially affect every cell in the body and produce a wide spectrum of effects depending on tissue concentration and cell type. A variety of glucocorticoids have been developed in an effort to vary the intensity and duration of effects and to decrease mineralocorticoid effects. However, systemic administration of these drugs is not a specifically targeted therapy and should be structured to minimize unwanted effects and to maximize therapeutic benefits.

Guidelines for use of glucocorticoids provided by product labeling range from broad to specific, depending on the product. A label may only state that a product is for use when an anti-inflammatory drug or adrenal glucocorticoid is needed or, alternatively, the label may list relatively specific indications for use. Many product labels state that treatment of conditions known to be responsive to anti-inflammatory glucocorticoids is indicated but then also list specific disorders for which the medication is known to be effective. For clarity, specific indications noted on product labeling are listed in this section as Accepted labeled indications and those not specifically named in U.S. or Canadian labeling are marked with an “US” or “US,CA” designation, respectively. However, it should be noted that products that are labeled for use in the treatment of general inflammation might also be considered efficacious in the treatment of more specific indications, such as musculoskeletal inflammation, for which it may not be listed because that specific type of inflammation is not mentioned on product labeling.

Accepted

Adrenocortical insufficiency, acute (treatment)—Glucocorticoids are indicated in the treatment of acute adrenocortical insufficiency (Addison’s disease); however, the mineralocorticoid effect will vary from product to product. For that small percentage of dogs with only glucocorticoid deficiency, long-term replacement can be performed without a need for mineralocorticoid; however, for the majority of dogs, mineralocorticoid replacement is necessary. Hydrocortisone, methylprednisolone, prednisolone, and prednisone produce minor mineralocorticoid effects in addition to their glucocorticoid effects and may adequately reverse electrolyte imbalances when administered in conjunction with intravenous sodium chloride solution; however, methylprednisolone, prednisolone, and prednisone are considered insufficient for long-term control of the potassium-retention or sodium and chloride losing effects of most cases of primary adrenocortical insufficiency and a mineralocorticoid-specific medication is generally indicated.

In acute adrenocortical insufficiency, a rapidly acting parenteral corticosteroid with the most mineralocorticoid effect available should be administered in conjunction with vascular volume expansion using isotonic saline. Relative mineralocorticoid effect from the most to the least potency is hydrocortisone > prednisolone/prednisone > methylprednisolone > dexamethasone.

Cats:

ELUS|Methylprednisolone tablets,
[ELUS] hydrocortisone tablets,
[ELUS] prednisolone sodium succinate injection,
[ELUS] prednisolone tablets,
and [ELUS] prednisone tablets are indicated in the treatment of acute adrenocortical insufficiency.

Dogs:

Prednisolone sodium succinate is indicated in the treatment of acute adrenocortical insufficiency when a rapid effect is necessary.

Horses:

Dexamethasone sodium phosphate is indicated for use in situations in which a rapid adrenocortical effect is needed; however, it provides no significant mineralocorticoid effect.

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Allergic disorders (treatment)—Many glucocorticoids are likely to be effective in the treatment of allergic reactions; however, the formulation should be chosen carefully to provide the onset of action, duration of action, and side effect profile to fit the type of reaction being treated. For example, for anaphylactic reactions, corticosteroids play a secondary role to epinephrine and fluid therapy. If corticosteroids are employed in the treatment of anaphylaxis, short-acting water soluble formulations are recommended.

Cats: Dexamethasone injection, methylprednisolone acetate injectable suspension, ELUS, methylprednisolone tablets, prednisolone sodium succinate, ELUS, triamcinolone acetonide injectable suspension, and ELUS, triamcinolone tablets are indicated in the treatment of allergic conditions.[R-7; 9; 14-16; 20; 22] Flumethasone, prednisolone, and triamcinolone tablets should also be effective in the treatment of allergic disorders.[R-100; 194]

Dogs: Dexamethasone injection, flumethasone injection, methylprednisolone acetate injectable suspension, ELUS, methylprednisolone tablets, prednisolone sodium succinate, ELUS, triamcinolone acetonide injectable suspension, and ELUS, triamcinolone tablets are indicated in the treatment of allergic conditions.[R-7; 9; 14-16; 17; 22] Prednisolone should also be effective in the treatment of allergic disorders.[R-100]

Horses: Dexamethasone injection, methylprednisolone acetate injectable suspension, and prednisolone sodium succinate are indicated in the treatment of allergic conditions.[R-7; 9; 18; 23; 24] Flumethasone injection, methylprednisolone and prednisolone should also be effective in the treatment of allergic disorders.[R-100; 194]

Pigs: Isolupredone acetate injectable suspension is indicated in the treatment of allergic conditions.[R-19] Although they are not labeled for use in cattle in the U.S., flumethasone, prednisolone, and prednisone should also be effective in the treatment of allergic disorders.[R-114]

Asthma, bronchial (treatment)—Cats: Methylprednisolone acetate injection or tablets, ELUS, prednisolone, or triamcinolone tablets are indicated in the treatment of bronchial asthma.[R-15; 19; 100] Once initial inflammation is controlled, other methods of controlling this disease should be pursued. If corticosteroid treatment must be continued, the lowest dose necessary and, if possible, alternate day therapy should be instituted.[R-215]

Colitis, ulcerative (treatment)—Dogs: Methylprednisolone tablets, prednisolone tablets, and prednisone tablets are indicated in the treatment of ulcerative colitis in dogs.[R-8; 100] However, use typically is reserved for cases that are not responsive to other therapies.

Inflammation, general (treatment)—Cats: Dexamethasone injection, methylprednisolone sodium succinate, prednisolone sodium succinate, methylprednisolone tablets, prednisolone tablets, elcan, triamcinolone acetonide injectable suspension, and elcan, triamcinolone tablets are indicated in the treatment of acute and chronic dermatoses of varying etiologies and the associated inflammation, irritation, and pruritis.[R-4; 9; 12; 14-18; 20; 22] Prednisolone tablets are labeled for the treatment of otitis externa.[R-10; 14-18]

Dogs: Dexamethasone injection, methylprednisolone sodium succinate, prednisolone sodium succinate, methylprednisolone tablets, prednisolone tablets, elcan, triamcinolone acetonide injectable suspension, and elcan, triamcinolone tablets are indicated in the treatment of acute and chronic dermatoses of varying etiologies and the associated inflammation, irritation, and pruritis.[R-4; 9; 12; 14-18; 20; 22; 28] Flumethasone injection, methylprednisolone acetate injectable suspension, elcan, methylprednisolone tablets, and elcan, prednisolone tablets, elcan, triamcinolone acetonide injectable suspension, and elcan, triamcinolone tablets are indicated in the treatment of acute and chronic dermatoses of varying etiologies and the associated inflammation, irritation, and pruritis.[R-4; 9; 12; 14-18; 20; 22; 28] Flumethasone injection, methylprednisolone acetate injectable suspension, elcan, methylprednisolone tablets, and elcan, prednisolone tablets are labeled for the treatment of otitis externa.[R-10; 14-18]

Disk disease, intervertebral (treatment)—Dogs: Dexamethasone injection and flumethasone injection are indicated as supportive therapy in the treatment of intervertebral disk disease (disk syndrome). However, it should be noted that high dosages of dexamethasone carry a risk of severe adverse effects.[R-380] Therapy should be tailored to the type of disk dysfunction and clinical signs. Elcan, methylprednisolone, prednisolone, or prednisone, administered at an anti-inflammatory dosage, may be a more appropriate choice of therapy in many cases.[R-2] However, acute paralysis due to intervertebral disk disease is an emergency usually requiring surgery and/or anti-inflammatory dosages much higher than those typically used for inflammation. For this form of the disease, see Spinal cord trauma, acute listed in this section.

Inflammation, musculoskeletal (treatment)—Corticosteroids are
indicated for symptomatic treatment of musculoskeletal disorders by reduction of pain, inflammation, and swelling. Clinical response is limited by the degree of irreversible pathologic change.

**Cats:** Dexamethasone injection, ELUS,CAN dexamethasone oral powder, ELUS,CAN flumethasone injection, and isoflupredone acetate injection are indicated in the treatment of joint and musculoskeletal inflammation. Although they are not labeled for use in cats in the U.S., ELUS,CAN methylprednisolone tablets, ELUS,CAN prednisolone tablets, ELUS,CAN triamcinolone acetonide injectable suspension, and ELUS,CAN triamcinolone tablets are indicated in the treatment of joint and musculoskeletal inflammation. **(R-8; 14; 18)**

Although they are not labeled for use in cattle in the U.S., ELUS,CAN methylprednisolone tablets, ELUS,CAN prednisolone tablets, ELUS,CAN triamcinolone acetonide injectable suspension, and ELUS,CAN triamcinolone tablets are indicated in the treatment of joint and musculoskeletal inflammation. **(R-4; 23; 24; 185)**

Although not labeled for use in pigs, ELUS,CAN methylprednisolone tablets, ELUS,CAN prednisolone tablets, ELUS,CAN triamcinolone acetonide injectable suspension, and ELUS,CAN triamcinolone tablets are indicated in the treatment of joint and musculoskeletal inflammation. **(R-16; 17)**

Although not labeled for use in cattle in the U.S., flumethasone, methylprednisolone, and prednisone should also be effective in the treatment of musculoskeletal inflammation. **(R-197)**

**Dogs:** Dexamethasone injection, ELUS,CAN dexamethasone tablets, ELUS,CAN flumethasone injection, methylprednisolone acetate injectable suspension, ELUS,CAN methylprednisolone tablets, ELUS,CAN prednisolone acetate injectable suspension, ELUS,CAN prednisolone tablets, ELUS,CAN triamcinolone acetonide injectable suspension, ELUS,CAN triamcinolone tablets, and ELUS,CAN triamcinolone tablets are indicated in the treatment of joint and musculoskeletal inflammation. **(R-4; 7; 10; 15-18; 22-46; 170)**

Although not labeled for use in pigs in the U.S., dexamethasone, flumethasone, methylprednisolone, and prednisone should also be effective in the treatment of ocular inflammation. **(R-47)**

**Horses:** Dexamethasone, flumethasone, prednisolone acetate injectable suspension and prednisolone sodium succinate are indicated in the treatment of inflammatory conditions of the eye. **(R-7; 9; 23)**

**Ketosis (treatment)—Cattle:** Dexamethasone injection, ELUS,CAN dexamethasone sodium phosphate injection, ELUS,CAN dexamethasone oral powder, ELUS,CAN flumethasone injection, isoflupredone acetate injection, methylprednisolone acetate injectable suspension, methylprednisolone tablets, prednisolone acetate injectable suspension, and prednisolone sodium succinate are indicated in the treatment of inflammatory conditions of the eye. **(R-15; 16; 17)**

Although not labeled for use in pigs, ELUS,CAN methylprednisolone, ELUS,CAN prednisolone, and ELUS,CAN prednisone should also be effective in the treatment of ocular inflammation. **(R-23)**

**Pigs:** Isoflupredone acetate injectable suspension is indicated in the treatment of inflammatory conditions of the eye. **(R-6; 16)**

**Shock, septic (treatment adjacent)—**The primary treatment of septic shock (endotoxemia) includes antimicrobial therapy and supportive parenteral fluid therapy. In the search for other medications to block the mediators of endotoxemic shock, a wide variety of research has been done, often with contradictory results. **(R-4; 7-52)** The use of glucocorticoids in the treatment of septic shock is therefore controversial and several criteria must be met for treatment to possibly be effective. High doses of a rapidly-acting glucocorticoid, preferably of short duration, should be given in conjunction with fluid and electrolyte therapy within a short period of time, possibly less than 1 hour, after the onset of sepsis. **(R-12; 63; 65; 70)** Because studies have shown flunixin to be at least as effective as or superior to glucocorticoids in the treatment of...
Cats: Methylprednisolone acetate injectable suspension is indicated in the treatment of septic shock; however, the rapid-acting corticosteroid formulations, such as dexamethasone sodium phosphate and prednisolone sodium succinate, are recommended as superior therapeutic choices in the treatment of endotoxic shock (septic shock) when administered as an adjunct to treatment with intravenous fluids and antibiotics.

Dogs: Methylprednisolone acetate injectable suspension is indicated in the treatment of septic shock; however, the rapid-acting corticosteroid formulations, such as dexamethasone sodium phosphate and prednisolone sodium succinate, are recommended as superior therapeutic choices in the treatment of endotoxic shock (septic shock) when administered as an adjunct to treatment with intravenous fluids and antibiotics.

Cattle and pigs: Isoflupredone acetate injectable suspension is indicated in the treatment of septic shock; however, the rapidly acting corticosteroid formulations, such as dexamethasone sodium phosphate, are recommended as superior therapeutic choices in the treatment of endotoxic shock (septic shock) when administered as an adjunct to treatment with intravenous fluids and antibiotics.

Horses: Isoflupredone acetate injectable suspension is indicated in the treatment of septic shock; however, the rapid-acting corticosteroid formulations, such as dexamethasone sodium phosphate, are recommended as superior therapeutic choices in the treatment of endotoxic shock (septic shock) when administered as an adjunct to treatment with intravenous fluids and antibiotics.

Abortion, induction of:

Cattle: Dexamethasone injection is used in the induction of abortion. It is generally administered after the 100th to 150th day of gestation, when prostaglandins administered alone are no longer effective. Although isoflupredone acetate can induce abortion when administered alone after the 100th day of gestation, it is not generally used in conjunction with a prostaglandin for the induction of abortion, as the use of isoflupredone acetate and a prostaglandin together is associated with an increased risk of fetal mummification, retained placentas, metritis, or endotoxemia in calves and ponies without the risk of attenuation of immune defenses, its use may be preferred in some situations.

Dexamethasone injection and dexamethasone sodium phosphate injection are used in the diagnosis of hyperadrenocorticism (Cushing’s syndrome) and differentiation of pituitary- versus adrenal-origin hyperadrenocorticism. The low-dose dexamethasone test is typically used for screening. The high-dose dexamethasone test has been used for differentiation of pituitary- versus adrenal-origin hyperadrenocorticism. The low-dose test is approximately 90% accurate in screening for hyperadrenocorticism and possibly 61% accurate in differentiation of pituitary- from adrenal-disease. The high-dose dexamethasone test is 75 to 80% accurate in differentiating the two forms of this disorder.

Horses: Dexamethasone injection is used in the diagnosis of pituitary pars intermedia-dependent hyperadrenocorticism.

Lupus erythematosus, systemic (treatment)
Dogs: Methylprednisolone, prednisolone, and prednisone are used in the treatment of systemic lupus erythematosus.

Lymphoma (treatment adjunct)
Cats and dogs: Prednisolone and prednisone are used in the treatment of lymphoma.

Parturition, induction of
Cattle: Dexamethasone and flumethasone have been used in the induction of parturition. However, only dexamethasone is labeled for use in cattle in the U.S. Parturition may be induced in the last few weeks of gestation to speed the onset of lactation or to control timing of parturition and involves much less risk to the fetus than earlier termination of pregnancy. Administration of corticosteroids more than 1 month before expected gestation often leads to poor neonatal survival, but may be necessary in some situations. Induction of parturition requires a knowledge of breeding date and is generally accomplished with administration of a glucocorticoid in conjunction with a prostaglandin to produce a predictable response time. In cattle, retained placentas are a common sequela to steroid-induced labor even when glucocorticoids are administered with prostaglandin (61% or more retained). The administration of a longer-acting glucocorticoid, such as triamcinolone, a week before induction may reduce the incidence of retained placentas (in one study, reduced to 14% retained); however, in 40% of cows, the triamcinolone preelection itself can induce parturition before the induction dose administered 6 days later takes effect.

Sheep: Dexamethasone and flumethasone have been used in the induction of parturition, however, these products are not labeled for use in sheep in the U.S.

Pemphigoid (treatment)

Cats and dogs: Prednisolone and prednisone have been used in the treatment of pemphigus diseases in cats and dogs and pemphigoid in dogs. When corticosteroids are used alone, they have been reported to be successful in controlling symptoms in approximately 40% of the cases treated. For animals not responsive to treatment with...
Prednisolone or prednisone alone, other immunosuppressive medications or aurothioglucose (gold salts) have been added to the treatment regimen.\cite{R39-42} The strength of evidence of efficacy of methylprednisolone succinate in cats leads clinicians to recommend use for this indication in dogs, also.

Thrombocytopenia, immune-mediated (treatment)\cite{R39-42}—Dogs: Prednisolone\cite{R94} and prednisone\cite{R95} are used in the treatment of immune-mediated thrombocytopenia.\cite{R39-42} Other underlying causes of thrombocytopenia, such as infection, drug reactions, or neoplasia, should be ruled out to be certain therapy is appropriate.\cite{R94;95} In cases that are initially refractory to prednisolone, other immunosuppressive medications, such as vincristine or cyclophosphamide, may be added.\cite{R94}

**Potentially effective**

Mastitis, acute coliform (treatment adjunct)\cite{R28}—Cattle: Although some product labeling mentions the use of dexamethasone as supportive therapy in the treatment of mastitis,\cite{R28} the efficacy and safety have not been clearly established. Dexamethasone is used as adjunctive therapy in the treatment of selected cases of acute coliform mastitis\cite{R141;142} because it can relieve some of the systemic signs due to endotoxin produced by Escherichia coli bacteria and reduce the significant mammary gland inflammation that is the hallmark of some acute cases.\cite{R145;144} Dexamethasone is considered adjunctive therapy only and should be administered in conjunction with primary treatments, such as intravenous fluids, antimicrobials, and an increased number of milkings a day.\cite{R142} Glucocorticoid therapy cannot be used in pregnant cows in middle- to late-gestation without risk of induction of abortion or parturition.\cite{R116-118;142}

Abortion, induction of\cite{R189}—Dogs: Although the safety and efficacy have not been established, the use of dexamethasone in the induction of abortion in dogs is supported by one uncontrolled study.\cite{R119} Frequent oral dosing for 10 days resulted in abortion in all treated dogs;\cite{R119} however, there is no other supporting information and clinical use is not reported to be common.

Sheep: Although the safety and efficacy have not been established, dexamethasone has been used in the induction of abortion. However, early abortion at the 88th to 92nd day of gestation was induced in only 2 of 5 sheep by the administration of dexamethasone alone in one study.\cite{R172} Dexamethasone is not labeled for use in sheep in the U.S. or Canada.

Anemia, immune-mediated hemolytic (treatment)\cite{R118}—Horses: Although the safety and efficacy have not been established, dexamethasone has been used in the treatment of immune-mediated hemolytic anemia in horses, based on a case report of successful responses.\cite{R97}

Chronic obstructive pulmonary disease (treatment)\cite{R201}—Horses: Although the safety and efficacy have not been clearly established, dexamethasone, isoflupredone, prednisolone, prednisone, and triamcinolone have been used in the treatment of chronic obstructive pulmonary disease. Research studies are limited and give conflicting results on efficacy, perhaps due to variable severity of the disease and problems with diagnosis and evaluation.\cite{R199-200} Efforts to decrease environmental irritants are very important in the control of this disorder.\cite{R201-203} Bronchodilators are also often part of the therapeutic strategy.\cite{R134} The risk of side effects, such as adrenal suppression and, possibly, laminitis, with chronic systemic administration of corticosteroids to horses should be considered.\cite{R202}

Inflammation, neurologic (treatment)\cite{R204}—All species: The safety and extent of efficacy have not been established for the use of glucocorticoids in the treatment of many types of inflammation associated with the nervous system in domestic species, therefore use and dosing continues to be debated.\cite{R36-45} The goal of glucocorticoid administration is to decrease tissue edema, vasculitis, and inflammation and, for acute injuries, to prevent post-traumatic autodestruction of tissue. Although treatment of intervertebral disk disease in dogs is a labeled indication for dexamethasone injection and flunixin injection,\cite{R148;149} glucocorticoids are used also in many other types of acute and chronic nervous system disorders. Some evidence supports the efficacy of intravenous methylprednisolone, a rapidly acting glucocorticoid, in speeding the return of neurologic function when administered within an hour after experimental acute spinal cord trauma in cats.\cite{R46;91;92} Dexamethasone has been shown to decrease significantly the edema associated with induced brain tumors\cite{R28} but to have little effect on edema associated with induced trauma to the brain.\cite{R192} however, there is some evidence that methylprednisolone can improve recovery from neurologic dysfunction associated with brain trauma.\cite{R93} Dexamethasone has been shown to decrease tissue edema in induced spinal cord trauma in laboratory situations, but an improvement in clinical outcome of induced acute spinal cord trauma in cats has not been as consistently demonstrated as it has been for methylprednisolone.\cite{R46;44;45}

Glucocorticoids typically are used as adjunctive therapy in acute, subacute, and chronic neurologic inflammation and do not preclude the necessity for specific diagnosis and disorder-specific therapy. Caution should be used when administering glucocorticoids to animals that may have a neurologic disorder involving fungal or viral infection or in situations in which the benefits have been seriously questioned, such as acute closed-head injuries.\cite{R141}

Inflammatory bowel disease (treatment)\cite{R205}—Cats and dogs: Although the safety and efficacy have not been established, methylprednisolone, prednisolone, or prednisone have been used in the treatment of inflammatory bowel disease.\cite{R198} No controlled studies are available. Because the term inflammatory bowel disease encompasses a variety of syndromes with differing severity and probably even differing underlying causes, response to medication can vary.\cite{R198} Therapies such as diet control may be instituted in conjunction with a medication or a combination of medications.\cite{R199}

Respiratory distress syndrome (treatment)\cite{R206}—Calves: Although the safety and efficacy have not been established, the use of corticosteroids before birth in the prophylaxis of respiratory distress syndrome in premature calves is supported by a controlled study in which medication was administered 30 hours before premature cesarean.\cite{R217} Dexamethasone and flunixin have been shown to increase pulmonary surfactant in various species;\cite{R217;218} however, only dexamethasone is labeled for use in food-producing animals in the U.S.

Note: Product labeling in the U.S. and Canada includes the use of glucocorticoids\cite{R14-24} as supportive therapy in the treatment of various disorders, including fatigue, heat exhaustion, influenza, metritis, milk fever, perioperative problems, pneumonia, pyelonephritis, retained placenta, shipping fever, stress, and traumatic gastritis. Although glucocorticoids may be helpful in treating specific effects, such as inflammation, associated with these disorders and are used in selected cases, routine use is not recommended.

Glomerular disease (treatment)\cite{R190}—Cats and dogs: Although the use of prednisolone in the treatment of glomerular disease (nephrosis) is mentioned on U.S. product labeling,\cite{R4} the efficacy and safety of this use has not been established and is not recommended.\cite{R194} Immune-complex or immune-mediated glomerulonephritis is believed to exist in cats, dogs, and human beings but the use of glucocorticoids in the treatment of these...
disorders in animals has not yet been demonstrated to be beneficial.[R-174] There are no controlled studies with immunosuppressive doses in animals, but in one small retrospective study of dogs, an anti-inflammatory dose of prednisolone was not beneficial for glomerulonephritis and may have been detrimental.[R-175] The use of corticosteroids in the treatment of immune-mediated glomerulonephritis is not recommended.[R-174, R-175] Shock, cardiogenic (treatment adjunct)[R-19]; or shock, hemorrhagic (treatment adjunct)[R-19]—All species: Although U.S. and Canadian product labeling includes the use of glucocorticoids in the treatment of shock, there is insufficient data to confirm the safety and efficacy of this use in cardiogenic or hemorrhagic shock. In the U.S. and Canada, isoflupredone acetate injectable suspension is labeled for the treatment of shock in cattle, horses, and pigs.[R-23, R-19] Flumethasone injection is labeled for the treatment of shock in dogs.[R-18] The use of glucocorticoids in the treatment of cardiogenic and hemorrhagic shock continues in the face of conflicting research data.[R-83, R-84] The primary treatment of shock is the administration of large volumes of crystalloid solutions.[R-85, R-86] High doses of glucocorticoids may aid in reversing some of the effects of shock when administered in conjunction with intravenous fluids.[R-64, R-56] The rapidly acting corticosteroid formulations are labeled for use in a limited number of species but are recommended as a superior therapeutic choice when administered in conjunction with other supportive therapies.[R-213] These rapidly acting medications include dexamethasone, hydrocortisone, methylprednisolone, and prednisolone sodium succinate.

Unaccepted

Laminitis, acute (treatment)—Horses: Although product labeling for dexamethasone[R-19] and prednisolone sodium succinate[R-87] includes use in the treatment of acute laminitis, there is some concern that glucocorticoids can predispose horses to laminitis and may exacerbate established conditions; therefore, this use is no longer recommended in most cases.

Snakebite (treatment)—Cattle, dogs, and horses: Although product labeling in the U.S. and Canada includes the use of dexamethasone, isoflupredone acetate injectable suspension, methylprednisolone acetate, or prednisolone sodium succinate in the treatment of snakebite, this indication is too general to be accurate.[R-212] The venom transmitted in a poisonous snakebite will vary depending on the species and condition of the snake.[R-180] Depending on clinical circumstances, the use of glucocorticoids in the treatment of an animal that is the victim of a snakebite may be appropriate or extremely inappropriate. There are little data on the efficacy of glucocorticoids in the treatment of snakebite in animals, but routine use is not recommended in human snakebite victims, based on a lack of evidence of any advantage.[R-121] There is a general concern that glucocorticoids may mask signs while not improving outcome; however, they may be indicated if specific sequelae that are responsive to glucocorticoids occur.[R-111, R-175]

Cats: Although Canadian product labeling includes the use of flumethasone injection in the stimulation of appetite in cats,[R-185] clinical use does not suggest that debilitated animals experience an increase in appetite with corticosteroid administration.[R-194] Other medications, such as cyproheptadine or a benzodiazepine, are more accepted choices for this indication.[R-121]

Regulatory Considerations

U.S.—Dexamethasone injection and isoflupredone acetate injectable suspension are labeled for use in food-producing animals. See the Dosage Forms section for further information on withdrawal times.

Canada—Dexamethasone oral powder, dexamethasone injection, dexamethasone sodium phosphate, flumethasone injection, isoflupredone acetate injectable suspension, and prednisolone acetate injectable suspension are labeled for use in food-producing animals. See the Dosage Forms section for further information on withdrawal times.

Chemistry

Source: The natural corticosteroids can be taken from animal adrenal glands; however, they usually are synthesized.[R-51] Dexamethasone—A synthetic analog of prednisolone.[R-8]

Flumethasone—A chemical modification of prednisolone.[R-14] Methylprednisolone—A 6-methyl derivative of prednisolone.[R-14] Prednisolone—A synthetic dehydrogenated analogue of cortisone.[R-8]

Chemical name:


Molecular formula:


Molecular weight:

Prednisolone acetate—402.48.\textsuperscript{[R-29]}
Prednisolone sodium succinate—482.50.\textsuperscript{[R-29]}
Prednisone—376.44.\textsuperscript{[R-29]}
Triamcinolone—394.43.\textsuperscript{[R-29]}
Triamcinolone acetate—434.50.\textsuperscript{[R-29]}

**Description:**
Dexamethasone USP—White to practically white, odorless, crystalline powder. Melts at about 215º C, with decomposition.\textsuperscript{[R-183]}
Methylprednisolone USP—White to practically white, odorless, crystalline powder. Melts at about 225º C, with some decomposition.\textsuperscript{[R-183]}
Prednisolone Acetate USP—Practically insoluble in water; sparingly soluble in dehydrated alcohol, in chloroform, and in methanol.\textsuperscript{[R-183]}

**Pharmacology/Pharmacokinetics**
Note: Unless otherwise noted, the pharmacokinetics included in this section are based on intravenous administration of a single dose.

**Mechanism of action/Effect:** The primary role of endogenous corticosteroids is the maintenance of homeostasis. In order to carry out this function, they affect nearly every cell in the body, altering the function of multiple systems.\textsuperscript{[R-30]} The glucocorticoids affect protein, carbohydrate, and lipid balance, while the mineralocorticoids affect water and electrolyte balance.\textsuperscript{[R-35]} The actions of glucocorticoids are brought about by interaction with specific glucocorticoid receptors in and on the cell. Nonspecific effects may also be brought about at high doses by direct interaction with the cell membrane.\textsuperscript{[R-31]} The effects in widespread but are, in some cases, specific to cell type. Therapeutic goals usually take advantage of only a few of the effects produced by glucocorticoids.

**For specific indications**
Adrenocortical insufficiency—Corticosteroids complex with receptors specific to glucocorticoid or mineralocorticoid effects on the plasma membrane and in the cytoplasm of target cells.\textsuperscript{[R-31]} Some nonspecific effects may also occur with cell membrane contact alone at high hormone concentrations.\textsuperscript{[R-31]} When receptor binding occurs, the complex formed by the corticosteroid and its receptor moves into the nucleus where it alters the expression of specific genes and thereby changes the production of enzymes causing the reactions needed for the maintenance of homeostasis and prevention of hypoadrenal shock. Glucocorticoid effects include maintenance of fluid homeostasis, maintenance of adrenergic receptor responsiveness, inhibition of fibroblast proliferation, secretion of digestive enzymes and absorption of fats, and hematopoietic and cardiovascular system function.

Although the activity is insignificant in glucocorticoids other than hydrocortisone, prednisolone, and prednisone, mineralocorticoid effects include increased reabsorption of chloride, sodium, and water and increased excretion of calcium and potassium; extracellular fluid volume is increased.\textsuperscript{[R-30; 33]}

**Inflammation**—The exact mechanism of action for the glucocorticoids in decreasing inflammation is not known\textsuperscript{[R-14; 31]} but they decrease or prevent tissue responses to inflammatory processes,\textsuperscript{[R-30]} thereby reducing the symptoms of inflammation without affecting the underlying cause. They block the increase in permeability of capillaries that occurs in inflammation, thereby reducing the transport of protein and maintaining microcirculation.\textsuperscript{[R-31]}

Glucocorticoids contribute to cell membrane stability; they reduce inflammation by reducing the response to kinins and toxins and by decreasing the formation of histamine induced by cell injury.\textsuperscript{[R-31]} They alter the distribution and function of peripheral leukocytes, decreasing their numbers at the site of inflammation.\textsuperscript{[R-14; 31]} To accomplish this, they decrease the vascular adherence of neutrophils and decrease diapedesis, thus preventing neutrophils from reaching the site of inflammation.\textsuperscript{[R-16; 37]} They also decrease macrophage response to migration inhibiting factor.\textsuperscript{[R-30; 31]} In addition, glucocorticoids also decrease production of cytokines and other mediators.\textsuperscript{[R-120]}

**Immunosuppression**—In general, glucocorticoids are considered less immunosuppressive than anti-inflammatory,\textsuperscript{[R-7]} however, the spectrum of effects they produce can also be very effective in controlling the effects of immune-mediated disease. Prevention of inflammatory mediator release, inhibition of inflammatory cell migration to and response in the site, reduced capillary permeability, and the prevention of passage of immune complexes through endothelial and basement membranes all provide

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beneficial effect in immune-mediated disease. The functional capacity of monocytes, macrophages, and eosinophils is decreased via inhibition of the formation of interleukins, and virus-induced interferon synthesis is inhibited. The alteration of the movement and circulation of leukocytes may alter the immune response. Circulating neutrophilia and eosinopenia in many species, as well as the lymphopenia and monocytosis seen in some species in response to glucocorticoids, may affect immune response.

Cell-mediated immunity is more affected than humoral immunity and T-cells more than B-cells by the presence of glucocorticoids. Antibody production generally is inhibited only with high doses or with long-term administration.

Ketosis—Cattle: When a glucocorticoid is administered, the concentration of glucose in the blood is increased through the synthesis of glucose from amino acids (gluconeogenesis), a decrease in the synthesis of protein from amino acids, and altered lipid metabolism. Thereby satisfying the systemic demand for glucose and helping to prevent the metabolism of fats and production of ketones. Also, peripheral utilization of glucose is reduced and liver storage of glycogen is increased.

Spinal cord trauma, acute—Glucocorticoids may limit neural damage. Adrenal axis suppression—The administration of glucocorticoids for purposes other than physiologic replacement therapy in adrenal insufficiency will result in species-specific dose-dependent suppression of the hypothalamic-pituitary-adrenal axis. In most species, high serum concentrations of circulating endogenous circulating glucocorticoids inhibit the production of adrenocorticotropic hormone (ACTH) by the anterior pituitary gland, preventing the subsequent stimulation of cortisol production by ACTH. Because of various other feedback loops, the administration of exogenous glucocorticoids can suppress the synthesis and secretion of thyroid stimulating hormone, follicle-stimulating hormone, prolactin, and virus-inactivating hormone, and growth hormone. The suppression of the production of cortisol is species-dependent and also varies widely depending on the glucocorticoid, the dose, and the duration of therapy. Measurable suppression can last from one or two weeks to as long as several months and prevention of hypoadrenal crisis may require gradual withdrawal of medication. However, there are few reports of hypoadrenal crisis in animals. One source states that animals at risk are generally considered to be those that were on greater than physiological replacement dosing for more than 2 weeks, whose treatment was discontinued in the last 6 weeks, and that are under some form of physiologic stress, such as surgery.

Bone effects—Glucocorticoids inhibit osteoblasts and stimulate osteoclasts, thereby inhibiting bone healing.

Cardiovascular effects—Glucocorticoids have direct positive chronotropic and inotropic actions on the heart. They enhance vasoconstriction and decrease capillary permeability, including that induced by inflammation. Blood pressure is increased, most likely from vasoconstriction and increases in blood volume. Beta-adrenergic receptors are increased in number and affinity; their presence potentiates the effects of beta-adrenergic agonists on bronchial smooth muscle to the benefit of asthmatic patients.

Central nervous system (CNS) effects—Glucocorticoids are essential for normal adrenergic receptor sensitivity in the autonomic nervous system. CNS effects include mood and behavioral changes (euphoria in human experience), maintenance of alpha rhythm, diminished response to pyrogens, appetite stimulation, and lowering of the seizure threshold.

Gastrointestinal effects—Glucocorticoids decrease the absorption of calcium and iron from the gastrointestinal tract, aid in the absorption of fat, increase secretion of acid, pepsin, and trypsin, and alter the structure of mucin in human beings.

Glucose, lipid, and protein metabolism—Glucocorticoids enhance lipolysis and mobilize fatty acids from adipose tissue; however, they also stimulate appetite, which stimulates hyperinsulinemia and results in lipogenesis. Abnormal redistribution of fat can occur with long-term use. Glucocorticoids cause a decrease in synthesis of proteins and an increase in degradation. With prolonged use, muscle atrophy, thin skin, and delayed healing can result.

Absorption:

Oral—In the dog, prednisolone and prednisone are absorbed rapidly and reach significant serum concentrations in less than 30 minutes.

Parenteral—Esterification of a glucocorticoid affects its water and lipid solubility and the rate at which it is absorbed from the injection site. Succinate and phosphate esters are the most water-soluble esters and are rapidly absorbed from intramuscular, intravenous, or subcutaneous administration. Acetate and acetone esters are poorly water-soluble and result in slow and sustained absorption from intramuscular depot injections.

Note: In the cow, 95% of an intramammary dose of 40 mg of dexamethasone is absorbed systemically within 3 hours; less than 5% is recovered in the milk.

Bioavailability—Dexamethasone:

Intramuscular administration—

Cattle: 67%, with a dose of 0.1 mg per kg of body weight (mg/kg).

Horses: 67 to 72%, with a dose of 0.1 mg/kg.

Oral—Horses: 61 ± 19%, with a total dose of 10 mg.

Distribution: Volume of distribution—

Dexamethasone:

Cattle—Area: 1.1 to 1.2 liters per kg (L/kg).

Dogs—Area:

1.85 ± 1.16 L/kg, with a 0.01 mg/kg dose.

6.41 ± 2.75 L/kg, with a 0.1 mg/kg dose.

1.11 to 1.29 L/kg, with a 1 mg/kg dose.

Horses—

Area: 0.906 to 0.966 L/kg.

Steady state: 1.73 ± 0.48 L/kg.

Methylprednisolone: Dogs—

Area: 1.76 ± 0.55 L/kg.

Steady state: 1.69 ± 0.53 L/kg.
Methylprednisolone—In rabbits, prednisone is rapidly converted by hydrolysis or hepatic biotransformation to become active. Prednisolone acetate: Completely available as the prednisolone base after intramuscular administration. Prednisone acetate, must be converted to base form, in this case prednisolone, regardless of which is administered. Prednisolone and cortisone are prodrugs that must be converted by hydrolysis or hepatic biotransformation to become active.

Note: Because glucocorticoids act intracellularly, plasma half-life may not correlate well with the duration of biological effect.

### Intravenous administration:

**Dexamethasone**
- Cattle: 4.9 to 5.6 hours
- Dogs: 3.2 hours, with a 0.01 mg/kg dose
- 6.9 hours, with a 0.1 mg/kg dose
- 2 to 2.3 hours, with a 1 mg/kg dose
- Horses: 0.88 hour
- Hydrocortisone—Dogs: 0.91 ± 0.06 minutes

**Methylprednisolone**
- Cattle: 1.43 ± 0.32 hours
- Dogs: 1.35 ± 0.13 hours
- Horses: 2.87 ± 1.5 hours
- Rabbits: 1.82 hours
- Methylprednisolone—Rats: 2.1 hours

Prednisolone—Cattle: 3.61 ± 1.18 hours, administered as the sodium succinate ester.

### Protein binding:

- Dexamethasone—Rats: High (83%)
- Methylprednisolone—Rabbits: High (77%)
- Prednisolone—Dogs: Moderate to high (51 to 84%, dose-dependent)

### Biotransformation:

**Hepatic metabolism** is the main elimination pathway of corticosteroids in animals. In addition, many glucocorticoids are administered in a form that must undergo hydrolysis or hepatic biotransformation to become active. Prednisone and cortisol are produgs that must be converted by the liver to prednisolone and hydrocortisone, respectively, to have glucocorticoid activity. The glucocorticoid esters, such as prednisolone acetate, must be converted to base form, in this case prednisolone, to be active.

Prednisone/prednisolone—In dogs, prednisone is rapidly converted by the liver into prednisolone, and prednisolone is rapidly converted into prednisone, although peak serum concentrations are consistently twice as high for prednisolone as for prednisone regardless of which is administered. Hepatic metabolism of prednisone to active prednisolone is considered rapid enough and compared to prednisolone that the effects of the administered prednisone compared to prednisolone should not be significantly different in dogs without severe hepatic compromise.

Methylprednisolone/methylprednisolone—In rabbits, methylprednisolone is rapidly and reversibly converted to methylprednisolone. Plasma concentration of methylprednisolone is generally greater than methylprednisolone regardless of whether methylprednisolone or methylprednisolone is administered; however, methylprednisolone is only 67 ± 15% available from methylprednisolone in the rabbit.

From ester to the active base—Methylprednisolone acetate: Rapidly hydrolyzed in fresh blood in vitro to methylprednisolone with a half-life of hydrolysis of about 20 minutes in human beings, 1.4 minutes in cats, and 14 minutes in cattle. However, in the dog only 46% of an intramuscular dose of 4 mg/kg becomes available as methylprednisolone base.

Methylprednisolone sodium succinate: Only 43% of an intravenous dose becomes available as methylprednisolone base in the dog.

Prednisolone acetate: Completely available as the prednisolone base after intramuscular administration.

Prednisolone 21-sodium succinate: Appears to be immediately hydrolyzed to prednisolone in the horse after intravenous administration. Completely available as the prednisolone base after intramuscular administration.

### Half-life:

**Absorption**—Intramuscular administration:

- Dexamethasone—Cattle: 1.2 to 1.6 hours, with a dose of 0.1 mg/kg
- Methylprednisolone acetate—Dogs: 69 hours, with a dose of 4 mg/kg

**Distribution**—Intravenous administration:

- Dexamethasone—Cattle: 0.13 to 0.18 hour
- Dogs: 0.13 to 0.5 hour
- Prednisone—Dogs: 0.25 hour
- Monkeys: 0.55 hour

### Elimination:

Note: Because glucocorticoids act intracellularly, plasma half-life may not correlate well with the duration of biological effect.

**Intravenous administration**:

**Dexamethasone**
- Cattle: 4.9 to 5.6 hours
- Dogs: 3.2 hours, with a 0.01 mg/kg dose
- 6.9 hours, with a 0.1 mg/kg dose
- 2 to 2.3 hours, with a 1 mg/kg dose
- Horses: 0.88 hour
- Hydrocortisone—Dogs: 0.91 ± 0.06 minutes

**Methylprednisolone**
- Cattle: 1.43 ± 0.32 hours
- Dogs: 1.35 ± 0.13 hours
- Horses: 2.87 ± 1.5 hours
- Rabbits: 1.82 hours
- Methylprednisolone—Rats: 2.1 hours

**Prednisolone**—Cattle: 3.61 ± 1.18 hours, administered as the sodium succinate ester.

### Onset of action:

Due to the nature of the glucocorticoids, comparative measurement of action, such as anti-inflammatory effect, is difficult to quantify in terms of a specific time of onset and duration. However, knowledge of the relative speed of absorption may be used to make therapeutic decisions when a rapid response is needed.

**Parenteral**—Intravenous administration is the most rapid route and certain products have been developed specifically to allow for rapid intravenous utilization, such as the sodium phosphate and sodium succinate esters. However, these products will only act as rapidly as their base glucocorticoids, methylprednisolone or prednisolone may provide the most rapid effect. Intramuscular and subcutaneous administration also may be rapidly absorbed and utilized but possible absorption delays tend to make these routes less favored for emergency treatment.
Oural—Oral routes of administration can provide a fairly rapid onset of action. Prednisone produces high serum concentrations and presumably early glucocorticoid effects within 30 minutes after administration to dogs.\[R-198\]

**Concentrations:**

**Endogenous serum cortisol, baseline—**

*Cats*: Ranges from 3 to 82.8 nanograms per mL (nanograms/mL) (mean 17 ± 2.8).\[R-140; 159\]

*Cattle*: 3 to 15 nanograms/mL.\[R-78; 74; 75; 120\]

*Dogs*: 15.8 ± 8 nanograms/mL.\[R-82\]

*Horses*: 43 to 87 nanograms/mL.\[R-67; 121; 151; 178\]

*Sheep*: 6.2 to 6.9 nanograms/mL.\[R-76\]

Note: In many species, endogenous serum cortisol has been described as cyclicly influenced by photoperiod. In horses, serum cortisol has been measured as lowest at 8 p.m. and highest at 8 a.m. with a significant difference consistently measured between the high and low values. In cats and dogs, there is no evidence that cortisol concentrations vary in a circadian pattern.\[R-55; 150; 208; 209\]

**Peak serum concentration—**

**Dexamethasone:**

*Intramuscular administration—Cattle*: 42 to 44 nanograms/mL at 3.6 to 4.3 hours after a dose of 0.1 mg/kg.\[R-170\]

*Intravenous—Horses*: 20 to 35 nanograms/mL at 15 minutes after a total dose of 5 mg per animal.\[R-40\]

*Oral—Horses*: 4.9 ± 0.17 nanograms/mL at 1.3 ± 0.5 hours, with a total dose of 10 mg per animal.\[R-60\]

**Prednisolone:**

*Intramuscular—*

*Cattle*: 1.2 mcg/mL at 8 minutes after a dose of 0.6 mg/kg, administered as the prednisolone 21-sodium succinate ester.\[R-74; 121\]

*Horses*: 59 ± 13.5 nanograms/mL at 10 hours\[R-67\] after a dose of 0.6 mg/kg, administered as the prednisolone acetate ester.

*Oral—Dogs*: 242 nanograms/mL at 0.9 hours after a total dose of one 5-mg tablet per animal (0.53 to 0.29 mg/kg).\[R-140\]

**Prednisone**

*Oral—Dogs*: 205 nanograms of prednisone per mL at 1.3 hours after a total dose of one 5-mg tablet per animal (0.53 to 0.29 mg/kg).\[R-140\]

Note: Peak serum prednisolone concentrations were always approximately twice as high as peak serum prednisone concentrations, regardless of whether oral prednisolone or prednisone was administered;\[R-140\] however, the combined prednisone and prednisolone areas under the serum concentration–versus–time curves were similar for oral prednisone and prednisolone administration.\[R-140\]

**Peak concentrations, other—Intra-articular administration:**

**Methylprednisolone acetate—**

*Cattle*: Serum methylprednisolone—7.8 ± 5.7 nanograms/mL at 4.5 ± 1.3 hours, with a total dose of 200 mg per animal (single joint treated).\[R-120\]

*Synovial methylprednisolone—*4 mg/mL at 20 minutes, with a total dose of 200 mg per animal (single joint treated).\[R-120\]

**Horses:**

*Serum methylprednisolone—*Less than 5 nanograms/mL for the first 24 hours after intra-articular administration, with a total dose of 110 mg.\[R-121\]

*Synovial methylprednisolone—*138 ± 83 mcg/mL at 2 hours and 174 ± 175 mcg/mL at 10 hours, with a total dose of 110 mg.\[R-121\]

Note: Although variable and not well defined, synovial methylprednisolone concentrations are detectable for up to 39 days (range 4 to 39 days).\[R-121\]

**Triamcinolone—**

*Cattle*: Serum triamcinolone—4.3 nanograms/mL at 4 hours, with a single dose of 6 mg.\[R-129\]

*Synovial triamcinolone—*7.5 mcg/mL 1 day after injection, with a single dose of 6 mg.\[R-129\]

Note: Synovial triamcinolone concentrations are detectable for up to 14 days.\[R-129\]

**Duration of action:** Some sources have considered the duration of anti-inflammatory effect of administered glucocorticoids to be similar in length to the duration of suppression of endogenous hormone and this is still used as a general indication of duration; however, the limitations of these measurements should be considered. It has been shown that some glucocorticoids, such as prednisone, can have readily apparent effects without changing measurable adrenocortical function.\[R-134\] In other situations, adrenocortical suppression may continue even though there are no longer measurable serum levels of other effects.\[R-135\] There are also species-specific and animal-specific variations in duration of action and in potency in treating a specific disorder.

The glucocorticoid bases, before their modification to form esters, have been classified into groups for description of duration of action for human beings, which may vary from duration in animals. This human classification lists cortisone and hydrocortisone as short-acting bases (8 to 12 hours)\[R-134\] Intermediate-acting bases (12 to 36 hours) include methylprednisolone, prednisolone, prednisone, and triamcinolone.\[R-58\] Long-acting bases (36 to 72 hours) include dexamethasone and flumethasone.\[R-51; 134\] The formation of esters from these bases can greatly alter solubility and rate of absorption, and, therefore, duration of action.

**Duration of suppression of endogenous cortisol concentrations:**

**Dexamethasone—**

*Cats*: Intravenous—Serum cortisol was suppressed below baseline concentration for 24 hours after a dose of 0.1 or 1 mg per kg of body weight (mg/kg).\[R-140\]

*Oral—*32 hours below detectable concentrations after a dose of 0.1 mg/kg.\[R-140\]

*Horses*: Intramuscular—2 to 4 hours of negligible cortisol concentration and 24 to 48 hours until a return to baseline, with a dose of 1 mg/kg.\[R-61\]

**Triamcinolone—**

*Horses*: Intramuscular—24 hours below detectable concentration and 4 to 7 days until a return to baseline after a dose of 0.05 mg/kg.\[R-67; 145\]

*Intravenous—*48 hours below baseline concentration after a dose of 0.2 mg/kg.\[R-151\] Suppression began 2 hours after administration.\[R-151\]

*Oral—*72 hours below baseline concentrations after a dose of 0.2 mg/kg.\[R-151\] Suppression began 2 hours after administration.\[R-151\]

**Pigeons:** Intravenous—Less than 24 hours below baseline concentration with a dose of 0.5 micrograms per kg of body weight (mcg/kg).\[R-146\]

52 hours below baseline concentration with a dose of 500 mcg/kg.\[R-146\]

*Methylprednisolone—**

*Cats*: Oral—Adrenocorticotropic hormone (ACTH) response was suppressed on the day after administration of 2 mg/kg every 12 hours for 1 week but had returned to normal 1 week after treatment was discontinued.\[R-139\]

*Methylprednisolone acetate—**

*Cattle*: Intravenous—6 weeks of below measurable or low concentrations and 11 weeks until a return to baseline after a dose of 200 mg of methylprednisolone acetate.\[R-126\]

*Oral—*days of below measurable or low concentrations and 11 weeks until a return to baseline after a dose of 200 mg of methylprednisolone acetate.\[R-126\]

*Horses*: Intramuscular—3 to 4 weeks below baseline concentration after administration of 2.5 mg/kg.\[R-135\]
Adrenal response to adrenocorticotropic hormone (ACTH) was suppressed for at least 5 weeks. Note: Even a subconjunctival injection of 10 mg/kg caused a suppression of endogenous cortisol starting 2 days later and a suppressed ACTH response for at least 9 days.

**Horses:** Intra-articular—6 to 18 hours below baseline concentration after an intra-articular injection of 120 mg as a total dose.

**Prednisolone**

- **Cattle:** Intramuscular or intravenous—2 days below baseline concentration after a prednisolone sodium succinate dose of 0.6 mg/kg.
- **Horses:** Intramuscular or intravenous—24 hours below baseline concentration after a dose of 0.6 mg/kg.
- **Pigeons:** Intravenous—Less than 24 hours below baseline concentration after a dose of 0.7 mg/kg.
- **Dogs:** Oral (4 weeks of therapy)—Dose of 0.22 mg/kg every 24 hours: For 2 of 8 dogs tested, serum cortisol was below the limits of the assay (1 mcg of cortisol per decaliter of serum) after 4 weeks of therapy. ACTH response was suppressed beginning 1 week after treatment and remained suppressed for most of the treatment period.
- **Horses:** Intramuscular—21 days below baseline concentration and 5 days at nondetectable or low concentrations after a dose of 0.6 mg/kg.
- **Prednisone—Dogs:** Oral (weeks of therapy)—Dose of 0.22 mg/kg every 24 hours: For 2 of 8 dogs tested, serum cortisol was below the limits of the assay (1 mcg of cortisol per decaliter of serum) after 4 weeks of therapy. ACTH response was suppressed beginning 1 week after treatment and remained suppressed for most of the treatment period.
- **Horses:** Intramuscular—21 days below baseline concentration and 5 days at nondetectable or low concentrations after a dose of 0.6 mg/kg.

**Prednisolone acetate**

- **Cattle:** Intramuscular—3 weeks below detectable concentrations and 6 weeks below baseline concentration after a prednisolone acetate dose of 0.6 mg/kg.
- **Horses:** Intramuscular—21 days below baseline concentration and 5 days at nondetectable or low concentrations after a dose of 0.6 mg/kg.

**Methylprednisolone**

- **Cattle:** Intramuscular—2 days below baseline concentration after a methylprednisolone sodium succinate dose of 0.6 mg/kg.
- **Horses:** Intramuscular—21 days below baseline concentration and 5 days at nondetectable or low concentrations after a dose of 0.6 mg/kg.

**Dexamethasone**

- **Total clearance:** Cattle—7.5 ± 0.83 mL/min/kg (prednisolone administered as the 21-sodium succinate ester).
- **Horses:** 8.4 mL/min/kg; 3.96 ± 0.96 mL/min/kg (administered as the sodium succinate ester).
- **Pigs—25.7 ± 2.1 mL/min/kg.

**Triamcinolone**—Elimination is equally divided between feces and urine after an intravenous dose of 2 mg/kg. Only 20% of injected radiolabeled triamcinolone is recovered as unchanged drug in the urine, although 90% of the injected drug is recovered in 120 hours.

**Precautions to Consider**

**Species sensitivity**

- **Mice, rabbits, and rats:** These species are considered steroid-sensitive because the administration of glucocorticoids causes a rapid lymphopenia induced by lymphocytolysis rather than the redistribution of circulating lymphocytes seen in other animal species, such as cattle, dogs, goats, horses, and pigs.

**Pregnancy/Reproduction**

**All species:** Corticosteroid administered systemically during the last trimester of pregnancy may induce the first stage of parturition. If induced prematurely, labor may be followed by dystocia, fetal death, retained placenta, and/or metritis. The likelihood of inducing abortion in ruminants is highest with the C16-methylated products, such as dexamethasone or flumethasone. Risk of abortion is still present but to a lesser degree with administration of isoflupredone or prednisolone.

**Dogs:** Offspring of dogs administered corticosteroids during pregnancy have had congenital anomalies, such as cleft palate, deformed forelegs, phocomelia (absence of the proximal part of a limb), or anasarca (generalized, massive edema). Corticosteroids administered during pregnancy have caused cleft palate.

**Lactation**

- **Cattle:** Dexamethasone—Dexamethasone concentrations in milk have been measured to be 0.3 to 0.5 times the plasma concentration in healthy cows. Dexamethasone was measurable in the milk 15 minutes after intravenous administration and concentrations declined at a rate similar to that in plasma. The half-life of 3 hours for elimination from the milk compares to 4.5 hours measured for plasma using an intravenous dose of 0.1 mg per kg of body weight (mg/kg).

- **Horses:** Intramuscular administration of dexamethasone crystalline suspension or a combination of sodium phosphate and long-acting phenylpropionate ester to ketotic cows at a dose of...
0.06 mg per kg of body weight (mg/kg) resulted in dexamethasone milk concentrations of up to 8.4 nanograms per mL, twelve hours after treatment. Three days after administration, milk dexamethasone concentrations had dropped to 1 nanogram per mL.\(^\text{[R-205]}\)

Flumethasone—Intramuscular administration of aqueous flumethasone at a dose of 0.014 mg/kg, to ketotic cows resulted in milk concentrations of flumethasone of 0.7 to 1.2 nanograms per mL, twelve hours after treatment.\(^\text{[R-205]}\)

Prednisolone—Less than 0.2% of an intravenous dose of 0.067 mg of prednisolone per kg of body weight is distributed into the milk in cows.\(^\text{[R-73]}\)

**Drug interactions and/or related problems**

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (\(\ast\) = major clinical significance):

- **Note:** Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

  - **Anti-inflammatory drugs, nonsteroidal (NSAIDs)**
    - in any species, the concurrent administration of glucocorticoids with nonsteroidal anti-inflammatory drugs may increase the risk of gastrointestinal irritation or ulceration
  - **Aspirin**
    - in the rat, aspirin lowers the half-life and increases the clearance of dexamethasone, probably by enhancing the hepatic metabolism;\(^\text{[R-401]}\) also, in any species, the concurrent administration of glucocorticoids with nonsteroidal anti-inflammatory drugs may increase the risk of gastrointestinal irritation or ulceration
  - **Norgestomet and estradiol valerate combination**
    - (flumethasone\(^\text{[R-119]}\) and possibly other corticosteroids can prevent or delay the generally predictable estrus in response to norgestomet and estradiol valerate in cattle)
  - **Phenytoin**
    - (in the rat, phenytoin suppresses the overall metabolism of dexamethasone, including decreasing the absorption rate and bioavailability and lowering the renal and plasma clearance, thereby increasing the half-life;\(^\text{[R-401]}\) also, in any species the concurrent administration of glucocorticoids with nonsteroidal anti-inflammatory drugs may increase the risk of gastrointestinal irritation or ulceration)
  - **Phenylbutazone**
    - (in the rat, phenylbutazone suppresses the overall metabolism of dexamethasone, including decreasing the absorption rate and bioavailability and lowering the renal and plasma clearance, thereby increasing the half-life;\(^\text{[R-401]}\) also, in any species the concurrent administration of glucocorticoids with nonsteroidal anti-inflammatory drugs may increase the risk of gastrointestinal irritation or ulceration)
  - **Vaccines**
    - (as in human beings, vaccination of animals that have been given immunosuppressive doses of corticosteroids is not recommended;\(^\text{[R-119]}\) short-term anti-inflammatory dosing of corticosteroids is not considered to interfere significantly with antibody response to vaccination;\(^\text{[R-265, 284]}\) although there is not a preponderance of research in this area)

**Human drug interactions and/or related problems**\(^\text{[R-2]}\)

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monograph *Corticosteroids*—

**Glucocorticoid Effects (Systemic) in USP DI Volume 1**: these drug interactions are intended for informational purposes only and may or may not be applicable to the use of corticosteroids in the treatment of animals:

- **Acetaminophen**
  - (induction of hepatic enzymes by corticosteroids may increase the formation of a hepatotoxic acetaminophen metabolite, thereby increasing the risk of hepatotoxicity, when they are used concurrently with chronic or high-dose acetaminophen therapy)
- **Aminoglutethimide**
  - (aminoglutethimide suppresses adrenal function so that glucocorticoid supplementation may be required; however, aminoglutethimide accelerates the metabolism of dexamethasone so that dexamethasone half-life may be reduced twofold; hydrocortisone is recommended instead because its metabolism is not known to be altered by aminoglutethimide and because its mineralocorticoid activity may also be required)
- **Amphotericin B, parenteral, or**
  - **Carbonic anhydrase inhibitors**
    - (concurrent use with corticosteroids may result in severe hypokalemia and should be undertaken with caution; serum potassium concentrations and cardiac function should be monitored during concurrent use)
    - (the use of hydrocortisone to control adverse reactions to amphotericin B has resulted in cases of cardiac enlargement and congestive heart failure)
    - (concurrent use of corticosteroids with acetazolamide sodium may increase the risk of hyponatremia and/or edema because corticosteroids cause sodium and fluid retention; the risk with corticosteroids may depend on the patient’s sodium requirement as determined by the condition being treated)
    - (the possibility should be considered that concurrent chronic use of both carbonic anhydrase inhibitors and corticosteroids may increase the risk of hypocalcemia and osteoporosis because carbonic anhydrase inhibitors also increase calcium excretion)
- **Anabolic steroids or**
  - **Androgens**
    - (concurrent use with glucocorticoids may increase the risk of edema; also, concurrent use may promote the development of severe acne)
- **Antacids**
  - (concurrent chronic use with prednisone or dexamethasone may decrease absorption of these glucocorticoids; efficacy may be decreased sufficiently to require dosage adjustment in patients receiving small doses, but probably not in those receiving large doses, of the corticosteroid)
- **Anticholinergics, especially atropine and related compounds**
  - (concurrent long-term use with glucocorticoids may increase intraocular pressure)
- **Anticoagulants, coumarin- or indandione-derivative, or**
  - **Heparin or**
  - **Streptokinase or**
  - **Urokinase**
    - (effects of coumarin or indandione derivatives are usually decreased [but may be increased in some patients] when these medications are used concurrently with glucocorticoids; dosage adjustments based on prothrombin time determinations may be necessary during and after glucocorticoid therapy)
    - (the potential occurrence of gastrointestinal ulceration or hemorrhage during glucocorticoid therapy, and the effects of glucocorticoids on vascular integrity, may cause increased risk to patients receiving anticoagulant or thrombolytic therapy)
- **Antidepressants, tricyclic**
  - (these medications do not relieve, and may exacerbate, corticosteroid-induced mental disturbances; they should not be used for treatment of these adverse effects)
- **Antidiabetic agents, oral, or**
  - **Insulin**
    - (glucocorticoids may increase blood glucose concentration; dosage adjustment of one or both agents may be necessary during concurrent use; dosage readjustment of the hypoglycemic agent may also be required when glucocorticoid therapy is discontinued)
- **Anti-inflammatory drugs, nonsteroidal (NSAIDs)**
  - (risk of gastrointestinal ulceration or hemorrhage may be increased when these substances are used concurrently with glucocorticoids; however, concurrent use of NSAIDs in the treatment of arthritis may provide additive therapeutic benefit and permit glucocorticoid dosage reduction)
Antithyroid agents or
Thyroid hormone
(changes in the thyroid status of the patient that may occur as
a result of administration, changes in dosage, or
discontinuation of thyroid hormones or antithyroid agents
may necessitate adjustment of corticosteroid dosage because
metabolic clearance of corticosteroids is decreased in
hypothyroid patients and increased in hyperthyroid patients;
dosage adjustment should be based on results of thyroid
function tests)
Asparaginase
(glucocorticoids, especially prednisone, may increase the
hyperglycemic effect of asparaginase and the risk of
neuropathy and disturbances in erythropoiesis; the toxicity
appears to be less pronounced when asparaginase is
administered following, rather than before or with, these
medications)
Cyclosporine
(seizures have been observed in patients receiving
cyclosporine and high doses of methylprednisolone)
Digitalis glycosides
(concurrent use with glucocorticoids may increase the
possibility of arrhythmias or digitalis toxicity associated with
hypokalemia)
Diuretic
(natriuretic and diuretic effects of these medications may be
decreased by sodium- and fluid-retaining actions of
corticosteroids, and vice versa)
Estrogens
(estrogens may alter the metabolism and protein binding of
glucocorticoids, leading to decreased clearance, increased
elimination half-life, and increased therapeutic and toxic
effects of the glucocorticoid; glucocorticoid dosage
adjustment may be required during and following concurrent use; monitoring of serum potassium concentration
is recommended)
Exenatide
(Folic acid
(requirements may be increased in patients receiving
long-term corticosteroid therapy)
Hepatic enzyme-inducing agents
(concurrent use may decrease the corticosteroid effect
because of increased corticosteroid metabolism resulting from
induction of hepatic microsomal enzymes)
Immunosuppressant agents, other
(concurrent use with immunosuppressant doses of
glucocorticoids may increase the risk of infection and
possibly the development of lymphomas or other
lymphoproliferative disorders; these neoplasms may be
associated with Epstein-Barr virus infections; a few studies in
organ transplant patients receiving immunosuppressant
therapy indicate that progression of the neoplasm may be
reversed after immunosuppressant dosage is decreased or
therapy is discontinued)
Isoniazid
(glucocorticoids, especially prednisolone, may increase
hepatic metabolism and/or excretion of isoniazid, leading to
decreased plasma concentration and effectiveness of
isoniazid, especially in patients who are rapid acetylators;
isoniazid dosage adjustment may be required during and
following concurrent use)
Mexilente
(concurrent use with glucocorticoids may accelerate
mexilente metabolism, leading to decreased mexilente
plasma concentration)
Mitotane
(mitotane suppresses adrenocortical function; glucocorticoid
supplementation is usually required during mitotane
administration, but higher doses than those generally used for
replacement therapy may be required because mitotane alters
glucocorticoid metabolism)
Neuromuscular blocking agents, nondepolarizing
(hypokalemia induced by glucocorticoids may enhance the
blockade of nondepolarizing neuromuscular blocking agents,
possibly leading to increased or prolonged respiratory
depression or paralysis [apnea]; serum potassium
determinations may be necessary prior to administration of
these agents)
Potassium supplements
(effects of these medications and/or corticosteroids on serum
potassium concentration may be decreased when these
medications are used concurrently; monitoring of serum
potassium concentration is recommended)
Salicylates
(although concurrent use with glucocorticoids may result in edema and increased blood pressure, possibly to
hypertensive levels)
(Salicylates may potentiate the antihypertensive effect
of these medications and/or corticosteroids on serum
corticosteroids may require sodium supplementation,
administration of live virus vaccines to patients receiving
inhibition of the growth response to somatrem or somatropin
these agents)
Somatrem or
Somatropin
(inhibition of the growth response to somatrem or somatropin
may occur with chronic therapeutic use of glucocorticoids
above certain doses)
Troleandomycin
(troleandomycin may decrease metabolism of
methylprednisolone and possibly other glucocorticoids,
leading to increased plasma concentration, elimination half-
life, and therapeutic and toxic effects; glucocorticoid dosage
adjustment may be required during and following concurrent
use)
Vaccines, live virus, or other immunizations
(administration of live virus vaccines to patients receiving
pharmacologic [immunosuppressant] doses of glucocorticoids
may potentiate replication of the vaccine virus, thereby
increasing the risk of the patient developing the viral disease,
and/or decrease the patient’s antibody response to the vaccine
and is not recommended; the patient’s immunologic status
should be evaluated prior to administration of a live virus
vaccine; also, immunization with oral poliovirus vaccine
should be postponed in persons in close contact with the
patient, especially family members)
(Other immunizations are not recommended in patients
Laboratory value alterations
The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (R = major clinical significance (possible effect in parentheses where appropriate)).

With diagnostic tests
Skin tests, intradermal
(dogs have significantly reduced responses to intradermally injected histamine phosphate solution for at least 6 days after a single intramuscular injection of 2.2 mg of prednisone per kg of body weight or 0.22 mg of triamcinolone per kg of body weight (R-

With physiology/laboratory test values
Adrenocortical function as assessed by ACTH stimulation or measurement of plasma or urinary free cortisol
(may be decreased with chronic glucocorticoid treatment (R-31)
Alkaline phosphatase (ALP) (R-147; 148) and
Gamma-glutamyltransferase (GGT) (R-147; 148)
(values may be increased in dogs, horses, and possibly other species)

Amylase, serum and
Lipase, serum
(in dogs, amylase may be increased or decreased; lipase may be increased without clinical pancreatitis (R-141)

Eosinophil count
(in dogs and other species, eosinopenia may occur (R-152; 153; 141)

Glucocorticoids—Glucocorticoid Effects (Systemic)
Volume I
Corticosteroids—Glucocorticoid Effects (Systemic) in USP DI

In addition to the above laboratory value alterations reported in animals, the following laboratory value alterations have been reported in humans, and are included in the human monograph
Due to other medications
Benozoate (high doses) or
Cyclosporine (high doses) or
Beta-agonists

Due to medical problems or conditions
Adrenal hyperfunction (Cushing’s syndrome) or
Carcinoma, disseminated, with concurrent serious infection or
Cardiac failure or
Dehydration or
Diabetes mellitus, unstable or
Fever or
Hypertension or
Malnutrition leading to extreme weight loss, recent or
Pregnancy or
Renal failure or
Temporal lobe disease

With other diagnostic test results
Brain imaging using sodium pertechnetate Tc 99m,
technetium Tc 99m gluceptate, or technetium Tc 99m pentetate
(uptake of these diagnostic aids into cerebral tumors may be decreased in patients receiving large doses of glucocorticoids because of glucocorticoid-induced reduction of peritumor edema)

Gonadorelin test for hypothalamic-pituitary-gonadal axis function
(glucocorticoids may alter the results of the gonadorelin test by affecting pituitary secretion of gonadotropins)

Nifedipine (high doses) or
Thyrotropin-releasing hormone test (TRH) and
Thyrotropin stimulation test (TSH) and
Thyroxine (T3) and
Fibrinogen

Protirelin test for thyroid function
(physiologic doses of corticosteroids have no effect, but pharmacologic doses may reduce the thyroid-stimulating hormone response to protirelin; however, withdrawal of corticosteroids in patients with known hypothyroidism is generally not recommended)

Skeletal imaging using technetium Tc 99m medronate,
technetium Tc 99m oxbindonate, or technetium Tc 99m pyrophosphate

receiving pharmacologic [immunosuppressant] doses of glucocorticoids because of the increased risk of neurological complications and the possibility of decreased or absent antibody response)
(immunizations may be administered to patients receiving glucocorticoids via routes or in quantities that are not likely to cause immunosuppression, for example, those receiving local injections, short-term [less than 2 weeks] therapy, or physiologic doses)

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The medical considerations/contraindications included have been:

- Infection, periarticular
- Fracture, intra-articular

Except under special circumstances, this medication should not be used when the following medical problems exist:

For all routes of administration

- Adrenal reserve
  - (signs of iatrogenic adrenal insufficiency should be monitored after long-term glucocorticoid therapy and the adrenocorticotropic hormone [ACTH] stimulation test may be performed during or after administration)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate) — not necessarily inclusive:

### Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; *s* = major clinical significance):

- Adrenal reserve
  - (signs of iatrogenic adrenal insufficiency should be monitored after long-term glucocorticoid therapy and the adrenocorticotropic hormone [ACTH] stimulation test may be performed during or after administration)

### Risk-benefit should be considered when the following medical problems exist:

For all routes of administration

- Abdominal surgery, extensive
- Bone fractures, severe or extensive
- Tissue damage, extensive, other
  - (corticosteroids can delay tissue healing and should be used with caution in patients with massive bone fractures or extensive abdominal surgery; if corticosteroids are used due to life-threatening events, a short- to intermediate-acting medication should be administered for the shortest period possible)

### Congestive heart failure
- (may be exacerbated; glucocorticoids have direct chronotropic and inotropic actions on the heart and also enhance vasoconstriction and decrease capillary permeability, thereby increasing blood pressure)

### Diabetes mellitus
- (glucocorticoids may increase insulin requirement)

### Renal function impairment
- (agents with mineralocorticoid effects may increase fluid retention and edema)

### Thrombophlebitis
- (may increase risk of thrombophlebitis)

### Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate) — not necessarily inclusive (*s* = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

**For intra-articular injection**

- Fracture, intra-articular
  - (healing may be retarded)
- Infection, periarticular
  - (intrasynovial, intratendinous, or other injections for local effect should not be performed when acute infections are present)

**For all routes of administration**

- Corneal ulcers
  - (may be exacerbated; the ability of the immune system to combat infections may be compromised with pharmacologic doses of glucocorticoids, particularly with systemic mycoses, mycobacterial infections, or infections that are refractory to therapy)

### Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; *s* = major clinical significance):

- Adrenal reserve
  - (signs of iatrogenic adrenal insufficiency should be monitored after long-term glucocorticoid therapy and the adrenocorticotropic hormone [ACTH] stimulation test may be performed during or after administration)

### Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate) — not necessarily inclusive:

### Those indicating need for medical attention

Incidence unknown

All species

- Allergic reactions, specifically anaphylactoid reactions; anorexia—uncommon; bone resorption or inhibition of bone growth; collagen synthesis inhibition; decreased growth rate; delayed bone and wound healing; diarrhea; suppression of endogenous steroid production; fever, reduced; gastrointestinal irritation/ulceration/perforation; hematopoietic changes; hypotension, acute — may occur with rapid parental administration of formulations containing polyethylene glycol or propylene glycol as a vehicle; hypertension; negative nitrogen balance; panting; potassium loss, sodium
Cats

- Diarrhea;
- Vomiting

Note: Although cats are reported to be more resistant to the effects of corticosteroids than dogs, there are few documented side/adverse effects, and the effects listed for dogs and all species are considered potential adverse reactions in cats.

Cattle

- Decreased milk production, temporary;
- Hypokalemia syndrome;
- Sperm defects;
- Termination of pregnancy

Note: Hypokalemia has been noted in cattle prone to anorexia or ketosis when treated with repeated doses of isoflupredone.

Dogs

- Adrenocortical atrophy;
- Alopecia;
- Calcinosus cutis;
- Diabetes mellitus;
- Diarrhea;
- Ecchymosis;
- Hepatopathy (hepatomegaly);
- Hyperadrenocorticism (Cushing’s syndrome;
- Hypoglycemia;
- Insulin resistance;
- Termination of pregnancy;
- Urinary tract infection

Note: After 2 weeks of oral prednisolone given at a dose of 0.55 mg per kg of body weight a day, dogs showed evidence of adrenocortical atrophy, fasting hyperglycemia, focal hepatocellular fatty changes, and skin atrophy.

The circumstances predisposing to the appearance of diabetes mellitus in dogs with iatrogenic or spontaneous hyperadrenocorticism are unclear; it is not known whether animals must have subclinical diabetes for the clinical disorder to occur or if glucocorticoids may potentially damage or alter beta cell function through induction of hyperglycemia. An additional factor may be the production of insulin resistance in tissues. Diabetes mellitus has been reported in a dog treated with methylprednisolone pulse therapy.

Hepatopathy or liver changes associated with glucocorticoid administration have been noted in some cases as early as the day after initiation of treatment, but the degree and pattern of the response varies. Hepatocytes become swollen and vacuolated and this initially may be due to hepatocellular accumulation of glycogen, or of some combination of components. Laboratory value alterations associated with glucocorticoid administration include increased serum gamma-glutamyltransferase, decreased serum gamma-glutamyltransferase, and normal to increased sulfobromophthalein sodium excretion test (BSP).

However, alterations in enzymes are not always proportional to degree of histologic change in hepatic tissue. Severe hepatocellular changes may be present before enzymes are significantly elevated. Although the predominance of ALP compared to the elevation of other enzymes is considered a marker of cholestasis, there is no evidence of cholestasis in dogs with steroid hepatopathy. The increased serum ALP activity has been shown to be the result of enzyme induction. Steroid hepatopathy is considered reversible in many dogs when corticosteroid therapy is ended, however, the return to normal may be
prolonged in some animals.\(^{[R-150]}\)

Chronic administration (≥ 35 days) of glucocorticoids in doses as low as those required for anti-inflammatory effects in dogs significantly changes the peripheral metabolism of thyroid hormones \(T_3\) and \(T_4\) by changing their binding to carrier proteins, altering their distribution, and by reducing \(T_3\) production from \(T_4^{[R-132]}\). Glucocorticoids also affect thyroid metabolism by affecting the hypothalamic-pituitary-thyroid axis.\(^{[R-133]}\)

Urinary tract infections are as likely to occur in dogs receiving long-term alternate-day anti-inflammatory therapy as in those treated daily.\(^{[R-165]}\)

Abnormal amylase and lipase values can occur in dogs in response to glucocorticoids without clinical pancreatitis.\(^{[R-140]}\) A definite connection between long-term corticosteroid administration and induction of clinical pancreatitis has not been demonstrated.\(^{[R-161]}\) The risk of pancreatitis may be increased by concurrent administration of a glucocorticoid with azathioprine.\(^{[R-127]}\)

**Horses**

- **Hepatopathy—rare;**\(^{[R-156]}\) laminitis—has been reported in association with dexamethasone, methylprednisolone, and triamcinolone administration;\(^{[R-22; 77; 109]}\) lethargy—doses higher than labeled doses;\(^{[R-96]}\) long, shaggy haircoat (hirsutism)\(^{[R-99]}\)

With intra-articular injections

- **Arthritis, septic;**\(^{[R-127]}\) increased inflammation (postinjection flare-up)\(^{[R-75; 16]}\)

**Rabbits**

- **Hepatopathy**

**Sheep**

- **Appetite, decreased;**\(^{[R-76]}\) thyroid hormone metabolism alterations—decreased plasma thyroxine;\(^{[R-140]}\) shedding of or slowed growth of wool—the decrease in wool growth and the amount of shedding is dose-related\(^{[R-76; 140]}\)

Those occurring principally after medication is discontinued, indicating need for medical attention

All species

- **Hypoadrenocorticism, acute**\(^{[R-28]}\) (lethargy, malaise, collapse, death)

Note: Rapid withdrawal of administered corticosteroids can lead to acute hypoadrenocorticism in animals with insufficient production of corticosteroids; however, because reports of this effect are rare, it is unknown how much risk occurs for most animals; animals undergoing sudden physiologic stress are believed to be most at risk of adrenal crisis.\(^{[R-4; 27; 136]}\)

**Human side/adverse effects**\(^{[R-2]}\)

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph Corticosteroids—Glucocorticoid Effects (Systemic) in USP DI Volume I; these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of corticosteroids in the treatment of animals:

- Incidence more frequent
  - Gastrointestinal irritation; increased appetite; indigestion; nervousness or restlessness; trouble in sleeping; weight gain

- Incidence less frequent or rare
  - Burning, numbness, pain, or tingling at or near injection site; changes in skin color or hypopigmentation; congestive heart failure—in susceptible individuals; diabetes mellitus; dizziness or lightheadedness; flushing of face or cheeks; generalized allergic reaction; headache; hiccups; increased joint pain—following intra-articular injection; increased sweating; infection at injection site; local allergic reaction; psychic disturbances such as delirium, disorientation, euphoria, hallucinations, manic-depressive episodes, mental depression, or paranoia; sudden blindness; vertigo

Note: Flushing of face or cheeks may persist for 24 to 48 hours.

**Hypopigmentation** is more likely at the injection site.

**Increased joint pain** may occur within a few hours postinjection and persist for up to 48 hours.

**Psychic disturbances** are more likely in patients with chronic debilitating illnesses that predispose them to psychic disturbances and in patients receiving higher daily dosages. Psychic disturbances may be related to dose rather than duration of therapy; symptoms may appear within a few days to 2 weeks after initiation of therapy and are usually associated with doses equivalent to 40 mg or more of prednisone per day. Additionally, euphoria or fear of relapse may lead to psychological dependence or abuse of corticosteroids.

**Sudden blindness** following injection into sites in the head or neck area, such as nasal turbinates or scalp, is due to possible entry of drug crystals into ocular blood vessels.

**For triamcinolone**

**Loss of appetite**

With intravenous administration

- **Anaphylaxis, generalized; cardiac arrhythmias; flushing of face or cheeks; seizures**

Note: Rapid intravenous administration of high doses of corticosteroids has been reported to cause convulsions, angioedema and/or anaphylactic reactions, and sudden death associated with cardiac arrhythmias. Monitoring of the electrocardiogram (ECG) is recommended. Equipment, medications, and trained personnel necessary for treating these complications should be immediately available.

Those occurring principally during long-term use indicating need for medical attention

- **Acne; adrenal suppression; avascular necrosis; cataracts, posterior subcapsular; Cushing’s syndrome effects, including filling or rounding out of face, hirsutism, hypertension, menstrual irregularities, muscle weakness, or striae; cutaneous or subcutaneous tissue atrophy—with frequent repository injections; ecchymosis; fluid and sodium retention; glaucoma with possible damage to optic nerves; growth suppression in children; hypokalemic syndrome; impaired wound healing; increased intracranial pressure; ocular infection, secondary, fungal or viral; osteoporosis or bone fractures—includes vertebral compression and long bone pathologic fractures; pancreatitis; peptic ulceration or intestinal perforation; scarring at injection site; steroid myopathy; tendon rupture; thin, fragile skin**

Those occurring principally after medication is discontinued, indicating a corticosteroid withdrawal syndrome

- **Withdrawal syndrome** (abdominal or back pain, dizziness, fainting, frequent or continuing unexplained headaches, low-grade fever, muscle or joint pain, nausea, prolonged loss of appetite, rapid weight loss, reappearance of disease symptoms, shortness of breath, unusual tiredness or weakness, vomiting)

Note: Too-rapid withdrawal of therapy, especially after prolonged use, may cause acute, possibly life-threatening, adrenal insufficiency and/or a withdrawal syndrome not related to HPA axis suppression.

Note: The risk of adverse effects with pharmacologic doses of corticosteroids generally increases with the duration of therapy and frequency of administration and, to a lesser extent, with dosage.

Chronic administration of physiologic replacement doses of corticosteroids rarely causes adverse effects.
Administration of glucocorticoids via local injection reduces the risk of systemic effects. The risk of both systemic and local adverse effects is still present to a degree, however, and increases with the frequency of injections.

Pharmacologic doses of glucocorticoids lower resistance to infection; the patient may be predisposed to systemic infections during, and for a time following, therapy. Increased susceptibility to infection may occur with short-term high-dose use (pulse therapy) as well as with more prolonged use. Also, symptoms of onset or progression of infections may be masked.

**Overdose**

For more information in cases of overdose or unintentional ingestion, contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center (888-426-4435 or 900-443-0000; a fee may be required for consultation) and/or the drug manufacturer.

Corticosteroids are synthesized hormones intended to act in a similar fashion to endogenous hormones; therefore, toxicity tends to occur in the midst of a variety of natural responses to therapy that the clinician may expect during treatment, particularly with higher doses. An overdose tends to be defined as the point at which adverse effects outweigh beneficial effects rather than a specific mg per kg of body weight dose known to cause a toxic reaction. The point at which the array of effects induced by hormones becomes an overdose varies among individual animals and among species. A single high dose may be intolerable or even fatal if an animal develops a severe effect, such as a perforated bowel, while another animal repeatedly given the same dose tolerates and benefits from the therapy with only minor side effects. Because side effects often occur and severe effects are not clearly predictable, some might define a toxicity situation as one in which an animal is on more medication than is minimally necessary to control disease and develops serious side effects.

**Clinical effects of overdose**

The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

- **Note:** The acute effects listed below may be associated with a short-term (1 to 4 days) high-dose administration.
- **Acute effects**
  - *All species*
  - Diarrhea; muscle weakness; polyuria/polydipsia; sodium and fluid retention and potassium loss—associated with medications that have mineralocorticoid effects
  - Chronic effects
  - *All species*
  - Hyperadrenocorticism (encompassing some or all of the side effects that can occur with pharmacologic glucocorticoid administration; see the Side/Adverse Effects section); vulnerability to hypoadrenal crisis—with cessation of therapy

**Treatment of overdose**

Discontinuation of therapy. Usually, a gradual withdrawal to avoid adrenal crisis is the primary treatment. When long-term treatment is essential to an animal, modification of dosing, such as alternate-day therapy, may be instituted to minimize adverse effects. Supportive treatment, such as medication to treat infection or gastrointestinal disorders, also may be necessary.

**Client consultation**

In providing consultation, consider emphasizing the following selected information:

- Following dosage and length-of-treatment recommendations
- Encouraging clients to communicate with the veterinarian about disease management, particularly in cases that require long-term therapy; noting the decrease in disease symptoms and the incidence of side effects in patients
- Risks of sudden withdrawal of medication after moderate- to long-term therapy

**Veterinary Dosing Information**

Because the glucocorticoids affect every cell in the body in often beneficial but potentially negative ways, it is important to administer these medications to produce the maximum positive effect necessary with the least side effects produced. The choice of dose of corticosteroid in the treatment of disorders in animals is inherently an empirical process. The clinician must individualize the dosage regimen using recommended guidelines for treatment of the disorder, the animal’s signalment and concurrent medical conditions, the animal’s response to medication, and other factors. The primary guideline is always the smallest dose for the shortest amount of time necessary to gain effective control of signs. However, for some difficult-to-control disorders, such as autoimmune diseases, high initial doses may be required until signs are controlled.

**Physiologic or replacement dosing is administered to hypoadrenal animals for maintenance.**

**Physiologic** therapy is the administration of corticosteroids at doses higher than natural levels of corticosteroids to produce a desired therapeutic effect—

- Anti-inflammatory dosing: Often the lowest pharmacologic doses are necessary to control inflammation and signs of allergies.
- Immunosuppressive dosing: Glucocorticoids are primarily anti-inflammatory medications and much higher doses are often required to control signs of immune-mediated disorders.
- Emergency, shock, or intensive short-term dosing: High-dose, short-term therapy is initiated to control hypoadrenal crisis, acute life-threatening inflammation, acute central nervous system (CNS) trauma, certain forms of CNS edema, and septic shock.

**Alternate-day therapy:** Changing the dosing interval from every 24 hours to every 48 hours once signs of disease are controlled has been called alternate-day therapy. It has been recommended to minimize adrenocortical suppression and other side/adverse effects of prolonged administration of glucocorticoids. For alternate-day dosing to be successful, the administration of glucocorticoids with a duration of action of 12 to 36 hours, such as prednisolone, prednisone, or methylprednisolone, is necessary. Originally, in order to change from daily to alternate-day dosing, it was recommended that the total dose given in a 48-hour period remain the same. For example, a dog given 20 mg of prednisolone a day would be gradually changed to 40 mg every other day. However, clinicians often combine the transition to a 48-hour dosing interval with tapering the dose in the treatment of some disorders. In the example given, the original 20-mg dose administered every 24 hours would be administered every 48 hours. The veterinarian chooses what type of transition to the longer dosing interval and/or lower dose is likely to be most successful, based on clinical history and, later, the response to initial changes in dosage. The goal of alternate-day dosing is to achieve a period within the 48-hour dosing interval when suppression of the adrenal axis is relieved. Alternate-day therapy can reduce adrenocortical suppression and decrease the effects of hyperadrenocorticism, but it will not completely prevent the eventual development of adverse effects. Among other things, the susceptibility to urinary tract infections may not be decreased. Also, alternate-day therapy may not work well for conditions requiring high doses because exacerbations can occur during the second day. However, this regimen should be considered whenever dosing is required for more than 2 weeks.

To begin alternate-day therapy, the animal must first be on therapy administered every 24 hours until good clinical results are achieved.

**Tapering dose:** In order to decrease adrenocortical suppression, tapering the dose to the minimum required to control signs is an
The glucocorticoids are all structural relatives of endogenous cortisol. When long-term glucocorticoid therapy is used, a protein-rich, potassium chloride–supplemented diet has been recommended to counteract nitrogen and potassium loss.

### Glucocorticoid product formulations

The glucocorticoids are all structural relatives of endogenous cortisol, produce similar effects, and in many situations requiring a glucocorticoid, they might be considered interchangeable when dose-adjusted for potency; however, because of the wide variation among medications in onset of action, duration of action, the amount of mineralocorticoid effect, and potency, there are preferred glucocorticoids for specific clinical situations. Similar animals may respond differently to the same dose of medication; therefore, the clinical response also helps define the dosage regimen.

The potency and duration of action depend on the structure of the glucocorticoid chosen for therapy.

<table>
<thead>
<tr>
<th>Basis</th>
<th>Potency*</th>
<th>Duration of action (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (hydrocortisone)</td>
<td>1</td>
<td>&lt;12</td>
</tr>
<tr>
<td>Cortisone</td>
<td>0.8</td>
<td>&lt;12</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
<td>12–36</td>
</tr>
<tr>
<td>Prednisone</td>
<td>4</td>
<td>12–36</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
<td>12–36</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>3–5</td>
<td>24–48</td>
</tr>
<tr>
<td>Isosflupredone</td>
<td>17</td>
<td>–</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>25–30</td>
<td>&gt;48</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25–30</td>
<td>&gt;48</td>
</tr>
<tr>
<td>Flumethasone</td>
<td>30</td>
<td>&gt;48</td>
</tr>
</tbody>
</table>

* Repeated high doses of some glucocorticoids with previously unreported mineralocorticoid effect may exacerbate electrolyte disturbances in susceptible animals. One example is clinical hypokalemia reported in some ketotic, postparturient cattle treated with multiple high doses of isosflupredone, in combination with other medications.

### Dexamethasone

#### Summary of Differences

- **Laboratory value alterations**: Dexamethasone can decrease serum testosterone in bulls and rams.
- **Lactation**: Dexamethasone concentrations in milk have been measured in cattle.
- **Pharmacology/pharmacokinetics**: Dexamethasone sodium phosphate is well-suited for rapid utilization when administered intravenously.
- **Side/adverse effects**: Dexamethasone has been associated with temporary sperm defects in cattle.
- **Veterinary dosing information**: In rats, dexamethasone has...
Drumstick is approximately 25 to 30 times the anti-inflammatory potency of cortisol and six to seven times the potency of prednisolone.\[R-38]\n
Dexamethasone has an insignificant amount of mineralocorticoid effect.\[R-38]\n
### Oral Dosage Forms

**Note:** The text between \[EL\] and \[ELUS\] describes uses not included in U.S. product labeling. Text between \[ELUCAN\] and \[EL\] describes uses that are not included in Canadian product labeling.

The \[EL\] or \[ELUCAN\] designation can signify a lack of product availability in the country indicated. See also the **Strength(s) usually available** section for each dosage form.

### DEXAMETHASONE ORAL POWDER

**Usual dose:**

\[ELUS\]Inflammation, including musculoskeletal inflammation\[EL—

Cattle and horses: Oral, 0.04 to 0.15 mg per kg of body weight a day.\[R-212]\n
**Note:** Product labeling lists a total dose of 5 to 10 mg per animal (approximately 0.01 to 0.02 mg per kg of body weight) a day for cattle.\[R-9\]

Extra-label withdrawal recommendations: Canada—Although dexamethasone oral powder is labeled for use in cattle, product labeling does not list an established meat or milk withdrawal time. There is some evidence that a significant withdrawal may necessary for this dexamethasone product under certain circumstances. Contact Canadian GFA RAD for recommendations (www.cgfarad.usask.ca, 866-243-2723).

**Note:** These products are not labeled for use in horses intended for food or in preruminating calves.\[R-13\]

**Strength(s) usually available:**\[R-13\]

**U.S.—**

Veterinary-labeled product(s):

Not commercially available.

Canada:

Veterinary-labeled product(s):\[R-3\]

10 mg per 15 grams of powder (Rx) [Dexone; GENERIC].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a well-closed container.

**USP requirements:** Not in USP.\[R-185\]

### DEXAMETHASONE TABLETS USP

**Usual dose:**

\[ELUS\]Dermatoses\[EL—

Inflammation, general, or

\[ELUS\]Inflammation, musculoskeletal\[EL—

Cats and dogs: Oral, 0.07 to 0.15 mg per kg of body weight a day for five to ten days or as appropriate for the disease condition.\[R-211\]

**Note:** \[ELUCAN\] Induction of abortion\[EL—

**Dogs:** Although the safety and efficacy have not been established for use in the induction of abortion, an oral dose of 0.2 mg per kg of body weight every ten hours for five days, followed by a tapering dose of 0.16 mg per kg of body weight every twelve hours on day six, 0.08 mg per kg of body weight every twelve hours on day seven, and 0.02 mg per kg of body weight every twelve hours on day eight has been used.\[R-118\]

For dogs more than 40 days into gestation, expulsion of fetuses is likely to occur, but for dogs between days 28 and 35 of gestation when medication is begun, a simple discharge is more often observed.\[R-118]\ In 60% of dogs treated, lethargy and depression may be noted during the abortion period.\[R-118\]

**Strength(s) usually available:**

**Note:** Human products have been listed for this dosage form based on relevance to veterinary practice.

**U.S.—**

Veterinary-labeled product(s):

0.25 mg (250 mcg) (Rx) [Dexium].

Human-labeled product(s):\[R-6\]

0.25 mg (250 mcg) (Rx) [GENERIC].

0.5 mg (500 mcg) (Rx) [Decadron; GENERIC].

0.75 mg (750 mcg) (Rx) [Decadron; Dexone; GENERIC].

1 mg (Rx) [GENERIC].

1.5 mg (Rx) [GENERIC].

2 mg (Rx) [GENERIC].

4 mg (Rx) [Decadron; GENERIC].

6 mg (Rx) [GENERIC].

**Canada—**

Veterinary-labeled product(s):\[R-12; 13\]

0.25 mg (250 mcg) (OTC) [Dextab].

Human-labeled product(s):\[R-5\]

0.5 mg (500 mcg) (Rx) [Dexason; GENERIC].

0.75 mg (750 mcg) (Rx) [Dexason; GENERIC].

4 mg (Rx) [Dexason; GENERIC].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a well-closed container.

**USP requirements:** Preserve in well-closed containers. Contain the labeled amount, within ±10%. Meet the requirements for Identification, Dissolution (70% in 45 minutes in dilute hydrochloric acid [1 in 100] in Apparatus 1 at 100 rpm), and Uniformity of dosage units.\[R-185\]

### Parenteral Dosage Forms

**Note:** The text between \[EL\] and \[ELUS\] describes uses not included in U.S. product labeling. Text between \[ELUCAN\] and \[EL\] describes uses that are not included in Canadian product labeling.

The \[EL\] or \[ELUCAN\] designation can signify a lack of product availability in the country indicated. See also the **Strength(s) usually available** section for each dosage form.

### DEXAMETHASONE INJECTION USP

**Usual dose:**

\[ELUS\]Allergic disorders\[EL—

Cats and dogs\[EL—

Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day.\[R-212\]

This dose may be repeated every twenty-four hours for three to five days\[R-4\] or as necessary for the disease condition.

**Cattle and horses:** Intramuscular or intravenous, 0.04 to 0.15 mg per kg of body weight a day.\[R-212\]

**Note:** Product labeling lists a total dose of 5 to 20 mg per animal (0.01 to 0.04 mg per kg of body weight) a day for cattle. These products are not labeled for use in preruminating calves.\[R-4; 6\]

See also the Extra-label withdrawal times section below.

**Dermatoses\[EL—

**Cats and dogs\[EL—

Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day.\[R-212\]

This dose may be repeated every twenty-four hours for three to five days\[R-4\] or as necessary for the disease condition.

**Disk disease, intervertebral\[EL—

**Dogs:** Intravenous, 0.07 to 0.15 mg per kg of body weight a day.\[R-212\]

**Note:** Because of a lack of research data on an effective dose of glucocorticoids in the treatment of disk disease in dogs, an anti-inflammatory dose is listed above, based on clinical judgment. This is not the dose or dosage form recommended for neurologic dysfunction or paralysis due to disk disease (see acute spinal trauma.

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under Methylprednisolone Sodium Succinate For Injection USP.

Inflammation, including musculoskeletal and ocular inflammation

Cats and dogs.* Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day. This dose may be repeated every twenty-four hours for three to five days or as necessary for the disease condition. Note: Product labeling lists a total dose of 5 to 20 mg per animal (0.01 to 0.04 mg per kg of body weight) a day for cats. These products are not labeled for use in preruminating calves. See also the Extra-label withdrawal times section below.

Horses: Intramuscular or intravenous, 0.04 to 0.15 mg per kg of body weight a day.

Cattle: Intramuscular or intravenous, 0.04 to 0.15 mg per kg of body weight a day.

Note: The above test recommendations are based on controlled studies in dogs.

Horses: Dexamethasone suppression test—After a baseline blood cortisol sample is taken, an intramuscular dose of 0.04 to 0.15 mg per kg of body weight is administered as a single dose. Blood cortisol samples are taken at four and eight hours postinjection. Normal adrenocortical suppression is typically defined as less than 1 mcg of cortisol per decaliter at twenty to twenty-four hours.

Note: The above test recommendations are based on controlled studies in horses.

Blood cortisol samples are taken at four and eight hours postinjection. Normal adrenocortical suppression is typically defined as less than 1 mcg of cortisol per decaliter at eight hours.

Note: The above test dose is based on a controlled study in cattle.

Cats:

Low-dose dexamethasone suppression test: After a baseline blood cortisol sample is taken, an intravenous bolus of 0.1 mg per kg of body weight is administered as a single dose. Blood cortisol samples are taken at four and eight hours postinjection. Normal adrenocortical suppression is typically defined as less than 1 mcg of cortisol per decaliter at four or eight hours postinjection or plasma cortisol < 1.4 mcg per decaliter at four or eight hours. However, specific values may vary depending on the laboratory.

Note: Although the safety and efficacy have not been established in the treatment of edema associated with brain tumors, in a controlled study an intramuscular dose of 3 mg per kg a day in divided doses has caused significant reduction of edema associated with induced tumors in dogs. However, it should be emphasized that corticosteroids have not been shown to be effective in trauma-induced cerebral edema although they may be of benefit in reducing tissue damage mediated by mechanisms other than cerebral edema.

Anemia, immune-mediated hemolytic**—Horses: Although the safety and efficacy have not been established in the treatment of immune-mediated hemolytic anemia, an intravenous or intramuscular dose of 0.3 to 1 mg per kg of body weight every twelve to twenty-four hours has been suggested. Once control of hemolysis is achieved, treatment...
is often switched to a corticosteroid more suitable for alternate-day therapy.

Extra-label withdrawal recommendations: U.S.—Although dexamethasone injection is labeled for use in cattle, product labeling does not list an established meat or milk withdrawal time. There is some evidence that a significant meat and milk withdrawal may be necessary for this dexamethasone product under certain circumstances. Contact the Food Animal Residue Avoidance Databank (FARAD, www.farad.org, 888-USFARAD) or the Canadian gFARAD (www.cgfarad.usask.ca, 866-243-2723) for recommendations.

Note: Canadian product labeling lists a total dose of 5 to 20 mg per animal (0.01 to 0.04 mg per kg of body weight) a day for cattle. {R-176}

These products are not labeled for use in horses intended for food or in prenuminating calves to be processed for veal. {R-4}

**Strength(s) usually available:** {R-13}

**U.S.—**

Veterinary-labeled product(s): {R-4; 6}

2 mg per mL (Rx) [Dexason; Dexam; GENERIC].

Canada—

Veterinary-labeled product(s):

Not commercially available.

**Packaging and storage:** Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by manufacturer. {R-4} Protect from freezing.

**USP requirements:** Preserve in light-resistant single-dose or multiple-dose containers, preferably of Type 1 glass. A sterile solution of Dexamethasone in Water for Injection. Label it to multiple-dose containers, preferably of Type I glass, protected from light. A sterile solution of Dexamethasone Sodium Phosphate in Water for Injection. Contains an amount of dexamethasone sodium phosphate equivalent to the labeled amount of dexamethasone phosphate, within –10% to +15%, present as the disodium salt.

**Dexamethasone Sodium Phosphate Injection USP**

Note: The dosing and strengths of the dosage forms available are expressed in terms of dexamethasone base (not the sodium phosphate salt).

4 grams of dexamethasone sodium phosphate equals 3.04 grams of dexamethasone base.

**Usual dose:**

Inflammation—

Dogs: Intravenous, 0.07 to 0.15 mg (base) per kg of body weight a day.

Horses: Intravenous, 0.01 to 0.15 mg (base) per kg of body weight a day.

Cats<sup>EL</sup>: Intravenous, 0.07 to 0.15 mg (base) per kg of body weight a day. The dose may be repeated daily if necessary.

Cattle<sup>EL</sup>: Intramuscular or intravenous, 0.04 to 0.15 mg (base) per kg of body weight a day. See also the Withdrawal times section below.

Hyperadrenocorticism (diagnosis)<sup>EL, CAN</sup>—Cats and dogs: See Dexamethasone Injection.

Ketosis<sup>EL</sup>—Cattle: Intramuscular or intravenous, 0.01 to 0.04 mg (base) per kg of body weight (5 to 20 mg total dose) a day. See also the Withdrawal times section below.

Septic shock<sup>EL</sup>—Cats, cattle, dogs, horses, and pigs:

Intravenous, 0.5 to 5 mg (base) per kg of body weight. See also the Withdrawal times section below.

**FLUMETHASONE**

**Summary of Differences**

Veterinary dosing information: Flumethasone has approximately 30 times the anti-inflammatory activity of cortisol and six to seven times the potency of prednisolone. Flumethasone has an insignificant amount of mineralocorticoid effect.

**Parenteral Dosage Forms**

Note: The text between ELUS and EL describes uses not included in U.S. product labeling. Text between ELCAN and EL describes uses that are not included in Canadian product labeling. The ELUS or EL CAN designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

**Flumethasone Injection**

**Usual dose:**

Note: The following doses are those included on product labeling for flumethasone; however, some members of the USP Veterinary Medicine Advisory Panel prefer the use of higher doses like those recommended for dexamethasone, a similarly potent glucocorticoid.

**Allergic disorders—**

Dogs: Intramuscular, intravenous, or subcutaneous, 0.0625 to 0.25 mg a day per animal, as a single dose. If necessary, the dose may be repeated.

Horses<sup>EL</sup>: Intramuscular or intravenous, 1.25 to 2.5 mg
Indications: Hydrocortisone is indicated in the treatment of

Dermatoses—

Cats: Intramuscular, intravenous, or subcutaneous, 0.03125 to 0.125 mg a day per animal, as a single dose. If necessary, the dose may be repeated.\[R-13; 185\]

Dogs: Intramuscular, intravenous, or subcutaneous, 0.0625 to 0.25 mg a day per animal, as a single dose. If necessary, the dose may be repeated.\[R-18; 185\]

Disk disease, intervertebral—

Dogs: Intramuscular, intravenous, or subcutaneous, 0.0625 to 0.25 mg a day per animal, as a single dose. If necessary, the dose may be repeated.\[R-18; 185\]

Inflammation, including musculoskeletal inflammation—

Dogs: Intramuscular, intravenous, or subcutaneous, 0.0625 to 0.25 mg a day per animal, as a single dose. If necessary, the dose may be repeated.\[R-18; 185\]

Horses: Intramuscular or intravenous, 1.25 to 2.5 mg per animal, as a single dose. If necessary, the dose may be repeated.\[R-18\]

Lactation—

Cows: Intramuscular or intravenous, 0.03125 to 0.125 mg a day per animal, as a single dose. If necessary, the dose may be repeated.\[R-18\]

Cattle—

Canadian product labeling lists an intramuscular or intravenous dose of 1.25 to 5 mg a day per animal as a single dose.\[R-18; 185\] If necessary, the dose may be repeated.\[R-18\]

Withdrawal times: US—This product is not labeled for use in food-producing animals in the U.S.; therefore there are no established withdrawal times. Canada—Meat: 4 days.\[R-18\]

Ketosis—

Cattle: Canadian product labeling lists an intramuscular or intravenous dose of 1.25 to 5 mg a day per animal as a single dose.\[R-18; 185\] If necessary, the dose may be repeated.\[R-18\]

Withdrawal times: US—This product is not labeled for use in food-producing animals in the U.S.; therefore there are no established withdrawal times. Canada—Meat: 4 days.\[R-18\]

Note: The use of a microsyringe or standard tuberculin syringe may be helpful in accurately administering small amounts of flumethasone.\[R-18\]

Strength(s) usually available—\[R-13\]

Usual dose:

ISOFLUPREDONE

Summary of Differences

Vernierdosing information: Isoflupredone has approximately 17 times the anti-inflammatory potency of prednisolone and four times the potency of prednisolone.

Parenteral Dosage Forms

Note: The text between ELUS and EL describes uses not included in U.S. product labeling. The ELUS or ELUS designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

ISOFLUPREDONE ACETATE INJECTABLE SUSPENSION USP

Usual dose: ISOFLUPREDONE ACETATE INJECTABLE SUSPENSION USP

Oral Dosage Forms

Note: Human products have been listed for this dosage form based on relevance to veterinary practice. The text between ELUS and EL describes uses not included in U.S. product labeling. Text between ELUS and ELUS describes uses that are not included in Canadian product labeling. The ELUS or ELUS designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

ISOFLUPREDONE

Summary of Differences

Vernierdosing information: Hydrocortisone or cortisol is the unit to which the anti-inflammatory and mineralocorticoid potencies of other corticosteroids are compared.

Oral Dosage Forms

Note: Human products have been listed for this dosage form based on relevance to veterinary practice. The text between ELUS and EL describes uses not included in U.S. product labeling. The text between ELUS and ELUS describes uses that are not included in Canadian product labeling. The ELUS or ELUS designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.
METHYLПREDNISИOLONE

Strength(s) usually available:

**U.S.—**

Veterinary-labeled product(s):[R-23; 24]
2 mg per mL (Rx) [Prefed 2X].

Canada—

Veterinary-labeled product(s):[R-23; 24]
2 mg per mL (Rx) [Prefed 2X].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Protect from freezing.

Incompatibilities: Isoflupredone should not be added to intravenous infusion solutions.[R-23]

USP requirements: Preserve in single-dose or multiple-dose containers, preferably of Type I glass. Label it to indicate that it is intended for veterinary use only. Contains the labeled amount, within ±10% to ±15%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, and pH (5.0–7.5), and requirements under Injections.[R-13; 183]

**METHYLПREDNISИOLONE**

Summary of Differences
Pharmacology/pharmacokinetics: Methylprednisolone sodium succinate is well-suited for rapid utilization when administered intravenously. Methylprednisolone acetate is well-suited for extended absorption when administered intramuscularly.

Veterinary dosing information: In mice, methylprednisolone has approximately five to six times the anti-inflammatory potency of cortisol and 1.5 times the potency of prednisolone.[R-26; 38] It has approximately one half the sodium-retaining effect of cortisol in mice.[R-38]

Oral Dosage Forms
Note: The text between EL and ELUS describes uses not included in U.S. product labeling. Text between ELUS and ELUS/ELUS describes uses that are not included in Canadian product labeling.

The ELUS designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

**METHYLПREDNISИOLONE TABLETS USP**

**Usual dose:**

**Canada—**

Adrenocortical insufficiency, acute—Cats and dogs: Oral, 0.1 to 0.25 mg per kg of body weight a day.[R-193; 206; 211]

**Allergic disorders:**

**Canada—**

**Dermatoses:** or

**Inflammation, including ocular and musculoskeletal inflammation—**Cats and dogs: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.[R-14]

Asthma—Cats: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.[R-14]

Colitis, ulcerative—Dogs: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.[R-14]

Note: A response is expected in 2 to 7 days, at which time the dose is reduced gradually. For acute disorders, the dose is tapered and discontinued. For chronic disorders, the minimal necessary dose for long-term maintenance is found.[R-14]

**Disk disease, intervertebral—**Dogs: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.

Note: Because of a lack of research data on an effective dose of glucocorticoids in the treatment of disk disease in dogs, an anti-inflammatory dose is listed above, based on clinical judgement. This is not the dose or dosage form recommended for neurologic dysfunction or paralysis due to disk disease (see acute spinal trauma under Methylпrednisolone Sodium Succinate For Injection USP).

**Lupus erythematosus—**Dogs: Oral, 2 to 4 mg per kg of body weight a day as an initial dose, which may be administered in divided doses. With a good response to treatment two weeks after initiation of therapy, the dose could be halved and four weeks after initiation the dosing interval may be doubled.[R-96; 99]

Note: The above dose is based on retrospective studies and case reports.

**Strength(s) usually available:**

**U.S.—**

Veterinary-labeled product(s):[R-23]
4 mg (Rx) [Medrol; GENERIC].

Canada—

Veterinary-labeled product(s): Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a tight container.

**USP requirements:** Preserve in tight containers. Contain the labeled amount, within ±7.5%. Meet the requirements for Identification, Dissolution (70% in 30 minutes in water in Apparatus 2 at 50 rpm), and Uniformity of dosage units.[R-140]
Parenteral Dosage Forms
Note: The text between ELCAN and ELUS describes uses not included in U.S. product labeling. Text between ELUS and ELCAN describes uses that are not included in Canadian product labeling.
The ELUS or ELCAN designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

METHYLPREDNISOLONE ACETATE INJECTABLE SUSPENSION USP
Usual dose:
Allergic disorders; or
Dermatoses—

Cats: Intramuscular, 10 to 20 mg as a total dose administered at an interval from one week to six months apart. The average total dose administered is 10 mg. The average total dose administered is 20 mg.

Dogs: Intramuscular, 2 to 120 mg as a single total dose (1.1 mg per kg of body weight). The average total dose administered is 20 mg.

Asthma—Cats: Intramuscular, 10 to 20 mg as a total dose administered at an interval from one week to six months apart.

Inflammation, including musculoskeletal inflammation—

Cats: Intramuscular, 10 to 20 mg as a total dose, administered at an interval from one week to six months apart. The average total dose administered is 10 mg. The average total dose administered is 20 mg.

Dogs: Intramuscular, 2 to 120 mg as a single total dose (1.1 mg per kg of body weight). The average total dose administered is 20 mg.

Horses: Intramuscular, 200 mg as a single total dose.

Withdrawal times: U.S. and Canada—Methylprednisolone acetate injectable suspension is not labeled for use in horses intended for food production.

Inflammation, musculoskeletal (joint)—

Dogs: Intrasynovial, 20 mg as a single total dose for large synovial spaces. The dose is decreased as the size of the joint space decreases.

Horses: Intrasynovial, 40 to 240 mg as a single total dose. The average dose is 120 mg. The dose is decreased as the size of the joint space decreases.

Withdrawal times: U.S. and Canada—Methylprednisolone acetate injectable suspension is not labeled for use in horses intended for food production.

Strength(s) usually available—

U.S.—Veterinary-labeled product(s):

20 mg per mL (Rx) [Depo-Medrol].

20 mg per mL (Rx) [Depo-Medrol].

Canada—Veterinary-labeled product(s):

20 mg per mL (OTC) [Depo-Medrol].

40 mg per mL (OTC) [Depo-Medrol; Methylprednisolone Acetate; Unimed; Vetacortyl; GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Protect from freezing.

Preparation of dosage form: See instructions on manufacturer labeling.

Stability: Reconstituted solution should be used within 48 hours.

USP requirements: Preserve in Containers for Sterile Solids. A sterile mixture of Methylprednisolone Sodium Succinate with suitable buffers. May be prepared from Methylprednisolone Sodium Succinate or from Methylprednisolone Hemisuccinate with the aid of Sodium Hydroxide or Sodium Carbonate. Contains an amount of methylprednisolone sodium succinate equivalent to the labeled amount of methylprednisolone, within ±10%, in the volume of constituted solution designated on the label. Meets the requirements for Constituted solution, Identification, Bacterial endotoxins, pH (7.0–8.0), in a solution containing about 50 mg of methylprednisolone sodium succinate per mL), Loss on drying (not more than 2.0%), Particulate matter, and Free methylprednisolone (not more than 6.6% of labeled amount of methylprednisolone), and for Sterility tests, Uniformity of dosage

than 75% are less than 10 micrometers in length, using 400x magnification), and for Injections.

METHYLPREDNISOLONE SODIUM SUCCINATE FOR INJECTION USP
Note: Human products have been listed for this dosage form based on relevance to veterinary practice.

The dosing and strengths of the dosage forms available are expressed in terms of methylprednisolone base (not the sodium succinate salt).

Usual dose: Spinal cord trauma, acute—Cats and dogs:

Intravenous, 15 to 30 mg (base) per kg of body weight, administered in a solution of 5% dextrose in water over one to several minutes. This dose has been effective when administered as an initial dose immediately after injury followed by a dose of 15 mg (base) per kg every eight hours and a tapered dose every eight hours over the week following the injury.

Note: The above dosing regimens are based on efficacy studies in cats with induced spinal trauma.

Some suggest that administering glucocorticoids for longer than six to eight hours after the spinal trauma occurs is nonproductive or even counterproductive.

Size(s) usually available:

U.S.—Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

40 mg (base) (Rx) [A-methaPred; Solu-Medrol; GENERIC].

125 mg (base) (Rx) [A-methaPred; Solu-Medrol; GENERIC].

500 mg (base) (Rx) [Solu-Medrol; GENERIC].

1 gram (base) (Rx) [Solu-Medrol; GENERIC].

2 grams (base) (Rx) [Solu-Medrol].

Canada—Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

40 mg (base) (Rx) [Solu-Medrol].

125 mg (base) (Rx) [Solu-Medrol].

500 mg (base) (Rx) [Solu-Medrol].

1 gram (base) (Rx) [Solu-Medrol].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a tight container. Protect from freezing.

Preparation of dosage form: See instructions on manufacturer labeling.

Stability: Reconstituted solution should be used within 48 hours.

USP requirements: Preserve in Containers for Sterile Solids. A sterile mixture of Methylprednisolone Sodium Succinate with suitable buffers. May be prepared from Methylprednisolone Sodium Succinate or from Methylprednisolone Hemisuccinate with the aid of Sodium Hydroxide or Sodium Carbonate. Contains an amount of methylprednisolone sodium succinate equivalent to the labeled amount of methylprednisolone, within ±10%, in the volume of constituted solution designated on the label. Meets the requirements for Constituted solution, Identification, Bacterial endotoxins, pH (7.0–8.0), in a solution containing about 50 mg of methylprednisolone sodium succinate per mL), Loss on drying (not more than 2.0%), Particulate matter, and Free methylprednisolone (not more than 6.6% of labeled amount of methylprednisolone), and for Sterility tests, Uniformity of dosage

Note: Human products have been listed for this dosage form based on relevance to veterinary practice.
PREDNISOLONE

Summary of Differences
Pharmacology/pharmacokinetics: Prednisolone sodium succinate\(^8\) has been developed specifically to allow for rapid onset of action, when administered intravenously.

Veterinary dosing information: Prednisolone has approximately four times the anti-inflammatory potency of cortisol and its potency equals that of prednisone.\(^{3; 16; 36}\) It has approximately 0.8 times the sodium-retaining effect of cortisol.\(^{3; 34}\)

Oral Dosage Forms
Note: The text between ELUS and ELUS-CAN describes uses not included in U.S. product labeling. Text between ELUS-CAN and EL describes uses that are not included in Canadian product labeling. The ELUS or ELUS-CAN designation may signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

PREDNISOLONE TABLETS USP
Usual dose:

**ELUS-CAN** Adrenocortical insufficiency, acute\(^8\)—

**Dogs** and **ELUS**\(^{31}\) Oral, 0.2 mg per kg of body weight a day.\(^{8; 100; 195; 196}\) This is the average dose administered to control signs, although clinicians may start with a higher initial dose of 0.3 to 0.4 mg per kg of body weight a day.\(^{8; 195}\) The dose is used in combination with mineralocorticoid replacement or alone in the treatment of secondary hypoadrenocorticism.\(^{195}\)

**ELUS** Oral, 0.1 to 0.5 mg per kg of body weight a day.\(^{8; 210; 211}\)

**ELUS-CAN** Allergic disorders\(^8\); or

**Dermatoses**—**Dogs** and **ELUS**\(^{31}\) Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.\(^{8; 38}\) Once clinical effect is achieved, the dose should be gradually reduced to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^{8; 38; 100; 193}\)

**ELUS-CAN** Inflammation, including ocular and musculoskeletal inflammations—**Dogs** Oral, 0.5 to 1 mg per kg of body weight every twenty-four hours as an initial dose.\(^8\) Once clinical effect is achieved, the dose should be gradually reduced to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^8\)

**ELUS**\(^{31}\) Oral, 2.2 mg per kg of body weight every twenty-four hours as an initial dose.\(^8; 195\) Once clinical effect is achieved, the dose should be gradually reduced to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^8; 195\)

**ELUS-CAN** Ulcerative colitis\(^8\)—**Dogs** Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.\(^8; 89\) Once clinical effect is achieved, the dose should be reduced gradually to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^8; 89\)

**ELUS-CAN** Anemia, autoimmune, hemolytic\(^8\)—**Cats and dogs** Oral, 1 to 3 mg per kg of body weight every twelve to twenty-four hours.\(^8; 39-41; 94; 98; 99\) Treatment is continued until the disease is controlled and, when clinically possible, changed to an alternate-day dose. A gradual decrease in dose to a maintenance therapy of 0.5 to 1 mg per kg of body weight every forty-eight hours is recommended.\(^8; 39-41\)

**ELUS**\(^{31}\) Asthma—**Cats** Oral, 2.2 mg per kg of body weight every twelve to twenty-four hours as an initial dose.\(^8; 28; 31; 100; 109\) Once clinical effect is achieved, the dose should be gradually reduced to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^8; 28; 31; 100; 109\)

**ELUS** Disk disease, intervertebral—**Dogs** Oral, 0.5 to 1 mg per kg of body weight every twenty-four hours as an initial dose.\(^8; 31; 109\) Once clinical effect is achieved, the dose should be gradually reduced to reach the lowest dose that is effective. Additionally, alternate-day therapy should be employed to reduce side effects.\(^8; 31; 109\)

Note: Because of a lack of research data on an effective dose of glucocorticoids in the treatment of disk disease in dogs, an anti-inflammatory dose is listed above, based on clinical judgment. This is not the dose or dosage form recommended for neurologic dysfunction or paralysis due to disk disease (see acute spinal trauma under Methylprednisolone Sodium Succinate For Injection USP).

**ELUS** Lupus erythematosus\(^8\)—**Dogs** Oral, 2 to 4 mg per kg of body weight a day as an initial dose, which may be administered in divided doses. With a good response to treatment, the dose could be halved, and four weeks after initiation the dosing interval may be doubled.\(^8; 90; 99\)

Note: The above dose is based on retrospective studies and case reports.

**ELUS** Lymphoma—**Cats and dogs** Oral, 2.2 mg per kg of body weight a day, administered in combination with chemotherapeutic medications effective in the treatment of lymphoma.\(^8; 83-86; 100; 108\) It is very uncommon for prednisolone to be administered as a sole agent because combination chemotherapy is often much more effective, and use of prednisolone alone is thought to make lymphoma less responsive to subsequent chemotherapy. The particular combination therapeutic regimen should be chosen based on initial evaluation of the animal and cancer staging, followed by subsequent evaluations.

**ELUS** Mast cell tumors—**Dogs** Oral, 1 mg per kg of body weight every twenty-four hours.\(^8; 100; 107\)

**ELUS** Pemphigus\(^8\); or

**ELUS** Pemphigus—**Dogs** Oral, 2 to 3 mg per kg of body weight every twelve hours.\(^8; 39-41\) After symptoms have been controlled, a maintenance dose of 1 to 2 mg per kg of body weight, administered every forty-eight hours, has been successful in continuing remission of signs in many animals that responded well to initial treatment with corticosteroids alone.\(^8; 39-41\)

Note: The above dose is based on dose-response trials and case reports.

**ELUS** Pemphigus—**Cats** Oral, 2 to 3 mg per kg of body weight every twelve hours.\(^8; 39-41\) After symptoms have been controlled, a maintenance dose of 2 mg per kg of body weight, administered every forty-eight hours, has been successful in continuing remission of signs in many animals that responded well to initial treatment with corticosteroids alone.\(^8; 39-41\)

Note: The above dose is based on dose-response trials and case reports.

**ELUS** Thrombocytopenia, immune-mediated—**Dogs** Oral, 2 mg per kg of body weight every twelve hours for seven to fourteen days.\(^8; 94\)

Note: In some cases that are refractory to treatment, other immunosuppressants, such as azathioprine or cyclophosphamide, are added to this regimen; however, it is controversial whether the combined therapy improves survival. The above dose is based on retrospective studies.

**ELUS** Chronic obstructive pulmonary disease—**Horses** Although the safety and efficacy have not been established, an
initial dose of 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours has been recommended for use in the treatment of chronic obstructive pulmonary disease. The dose should be tapered and, when feasible, discontinued. The strengths usually available:

U.S.—
   Veterinary-labeled product(s): [Rx]
   Human-labeled product(s): [Rx]
   5 mg (Rx) [PrednisTab]
   20 mg (Rx) [PrednisTab]

Canada—
   Veterinary-labeled product(s): Not commercially available.
   Human-labeled product(s): Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a well-closed container.

USP requirements: Not in USP.

PREDNISOLONE SYRUP USP

Usual dose:
   Human-labeled product(s):
   1 mg per mL (Rx) [Pediapred (sorbitol)]
   5 mg per mL (Rx) [Orapred (alcohol 1.8%, sorbitol)]

Veterinary-labeled product(s):
   5 mg per mL (Rx) [GENERIC]
   20 mg per mL (Rx) [Presnidolone Syrup]

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a tight container. Protect from light and from freezing.

USP requirements: Preserve in tight, light-resistant containers. Contains the labeled amount, within ±10%. Presnidolone Syrup may contain alcohol. Meets the requirements for Identification, pH (3.0–4.5), and Alcohol content (if present, within –10% to +15%).

Parenteral Dosage Forms

Note: The text between 51-5 and 51-6 describes uses not included in U.S. product labeling. Text between 51-5 and 51-6 describes uses that are not included in Canadian product labeling. The 51-5 designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

PREDNISOLONE ACETATE INJECTABLE SUSPENSION USP

Usual dose:
   Intramuscular or intravenous, 1 to 2 mg per kg of body weight
   as an initial dose, followed by equal maintenance doses
   at one-, three-, six-, or ten-hour intervals.

Strength(s) usually available:

U.S.—
   Veterinary-labeled product(s):
   5 mg per mL (OCT) [GENERIC]
   10 mg per mL (OTC) [GENERIC]
   50 mg per mL [Uni-Pred 50; GENERIC]

Canada—
   Veterinary-labeled product(s):
   10 mg per mL (OTC) [GENERIC]
   50 mg per mL [Uni-Pred 50; GENERIC]

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a well-closed container. Protect from freezing.

Auxiliary labeling: • Shake well before using.

USP requirements: Preserve in single-dose or in multiple-dose containers, preferably of Type I glass. A sterile suspension of Prednisolone Acetate in a suitable aqueous medium. Contains the labeled amount, within ±10%. Meets the requirements for Identification and pH (5.0–7.5), and for Injections.
continued for three to five days, if necessary.\textsuperscript{[R-7]}

**Dogs:** Intramuscular, 0.5 to 1 mg per kg of body weight.\textsuperscript{[R-9; 855]} The dose is repeated in twelve to twenty-four hours and continued for three to five days.\textsuperscript{[R-7]}

**Horses:** Intramuscular or intravenous, 0.25 to 1 mg per kg of body weight.\textsuperscript{[R-9]} If administered intravenously, the dose should be given slowly over thirty seconds to one minute.\textsuperscript{[R-7]} The dose should be repeated at twelve, twenty-four, or forty-eight hours, depending on clinical response.\textsuperscript{[R-9]}

**Packaging and storage:**

- **Cats:** Intramuscular, 1 mg per kg of body weight.\textsuperscript{[R-9]} The dose may be repeated in twelve to twenty-four hours and continued for three to five days, if necessary.\textsuperscript{[R-7]}
- **Dogs:** Intramuscular, 0.5 to 1 mg per kg of body weight.\textsuperscript{[R-9; 855]} The dose is repeated in twelve to twenty-four hours and continued for three to five days.\textsuperscript{[R-7]}

**Septic shock—**

**Cats, dogs, and horses:** Intravenous, 15 to 30 mg per kg of body weight as an initial dose.\textsuperscript{[R-403]} to be repeated in 4 to 6 hours.\textsuperscript{[R-61-66]} The intravenous dose should be administered slowly.\textsuperscript{[R-9]} Note: This treatment regimen should be administered with aggressive fluid therapy.

Note: \textsubscript{\textsuperscript{[R-7]}}

Immunosuppression\textsuperscript{[R-9]}—**Cats and dogs:** Although the safety and efficacy have not been established, an intramuscular or intravenous dose of 2 to 4 mg per kg of body weight a day for three or more days as needed to control the condition\textsuperscript{[R-9]} has been used for immunosuppression. The dose is then tapered to 2 to 4 mg per kg of body weight every forty-eight hours.\textsuperscript{[R-403]}

Strength(s) usually available: (When mixed according to manufacturer’s instructions)—

- **U.S.**
  - Veterinary-labeled product(s)—\textsuperscript{[R-7]}
    - 10 mg per ml (Rx) [Solu-Delta-Cortef].
    - 50 mg per ml (Rx) [Solu-Delta-Cortef].
  - Veterinary-labeled product(s)—\textsuperscript{[R-9]}
    - 10 mg per ml (Rx) [Solu-Delta-Cortef; GENERIC].
    - 50 mg per ml (Rx) [Solu-Delta-Cortef].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F) in a well-closed container, unless otherwise specified by the manufacturer. Protect from freezing.

Stability: Reconstituted product should be used immediately and should not be stored;\textsuperscript{[R-7]} any unused reconstituted product should be discarded.\textsuperscript{[R-7]} If the solution becomes cloudy after reconstitution, it should not be used intravenously.\textsuperscript{[R-7]}

Incompatibilities: Prednisolone sodium succinate should not be added to calcium infusion solutions.\textsuperscript{[R-7]}

USP requirements: Preserve in Containers for Sterile Solids. It is sterile prednisolone sodium succinate prepared from Prednisolone Hemisuccinate with the aid of Sodium Hydroxide or Sodium Carbonate. Contains suitable buffers. Contains an amount of prednisolone sodium succinate equivalent to the labeled amount of prednisolone, within ±10%. Meets the requirements for Constituted solution, Identification, Bacterial endotoxins, pH (6.7–8.0, determined in the solution constituted as directed in the labeling), Loss on drying (not more than 2.0%), and Particulate matter, and for Sterility tests, Uniformity of dosage units, and Labeling under Injections.\textsuperscript{[R-180]}

**PREDNISONE**

**SUMMARY OF DIFFERENCES**

Pharmacology/pharmacokinetics: Prednisone requires conversion by the liver to the active compound prednisolone. Hepatic metabolism of prednisone to prednisolone is considered rapid enough and the serum concentration versus time curves similar enough for the two medications that the effects of the administered prednisone are not significantly less than those of prednisolone\textsuperscript{[R-180]} in dogs without severe hepatic compromise.

Veterinary dosing information: In mice, prednisone has approximately four times the anti-inflammatory potency of cortisol and equals that of prednisolone.\textsuperscript{[R-16; 38]} It has approximately 0.8 times the sodium-retaining effect of cortisol in mice.\textsuperscript{[R-30]}

**ORAL DOSAGE FORMS**

Note: Dosing for prednisone is considered comparable to prednisolone in animals without severe liver disease.

The text between \textsuperscript{[R-16]} and \textsuperscript{[R-193]} describes uses not included in U.S. product labeling. Text between \textsubscript{\textsuperscript{[R-16]}} and \textsubscript{\textsuperscript{[R-193]}} describes uses that are not included in Canadian product labeling.

The \textsubscript{\textsuperscript{[R-16]}} designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

**PREDNISONE TABLETS USP**

Usual dose:

- **U.S.**
  - Adrenocortical insufficiency\textsuperscript{[R-11]; [R-38]}, Allergic disorders\textsuperscript{[R-11]}, Anemia, autoimmune, hemolytic\textsuperscript{[R-11]}, Asthma\textsuperscript{[R-11]}, Chronic obstructive pulmonary disease\textsuperscript{[R-11]}, Dermatosis\textsuperscript{[R-11]}, Disk disease, intervertebral\textsuperscript{[R-11]}, Inflammation\textsuperscript{[R-11]}, including ocular\textsuperscript{[R-11]} and musculoskeletal inflammation; Lupus erythematosus\textsuperscript{[R-11]}, Lymphoma\textsuperscript{[R-11]}, Mast cell tumors\textsuperscript{[R-11]}, Pemphigoid\textsuperscript{[R-11]}, Pemphigus\textsuperscript{[R-11]}, Thrombocytopenia, immune-mediated\textsuperscript{[R-11]}, or Ulcerative colitis—See Prednisone Tablets USP, above in this monograph, for dosage recommendations.

Strength(s) usually available: (When mixed according to manufacturer’s instructions)—

- **U.S.—**
  - Veterinary-labeled product(s):
    - Not commercially available.
  - Human-labeled product(s):
    - 1 mg (Rx) [GENERIC].
    - 2.5 mg (Rx) [GENERIC].
    - 5 mg (Rx) [GENERIC].
    - 10 mg (Rx) [GENERIC].
    - 20 mg (Rx) [GENERIC].
    - 50 mg (Rx) [GENERIC].
  - Veterinary-labeled product(s):
    - Not commercially available.
  - Human-labeled product(s):
    - 1 mg (Rx) [Apo-Prednisone).
    - 5 mg (Rx) [Apo-Prednisone; Novo-Prednisone; GENERIC].
    - 50 mg (Rx) [Apo-Prednisone; Novo-Prednisone; GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Store in a well-closed container.
TRIAMCINOLONE

Summary of Differences
Veterinary dosing information: Triamcinolone has approximately five times the anti-inflammatory potency of cortisol and 1.25 times the potency of prednisolone. It has no significant mineralocorticoid effect.

Oral Dosage Forms
Note: The text between {R-13} and {R-14} describes uses not included in U.S. product labeling. Text between {R-15} and {R-16} describes uses that are not included in Canadian product labeling.
The {R-15} or {R-16} designation can signify a lack of product availability in the country indicated. See also the Strength(s) usually available section for each dosage form.

TRIAMCINOLONE TABLETS USP
Usual dose:

{R-15}Allergic disorders{R-21};
{R-16}Dermatoses{R-21}; or
{R-15}Inflammation{R-21}, including musculoskeletal inflammation—
Cats and dogs: Oral, 0.5 to 1 mg per kg of body weight every twenty-four hours as an initial dose, then taper to 0.5 to 1 mg per kg of body weight every forty-eight hours. With acute, short-term conditions, as soon as clinical signs are controlled, the dose should be gradually reduced and then discontinued. In the case of chronic conditions, after a satisfactory clinical response the dose should be reduced until the minimum effective maintenance dose is reached.

Strength(s) usually available:{R-14}
U.S.—
Veterinary-labeled product(s){R-24}
0.5 mg (Rx) [Cortalone; Triacet; Triamtabs; GENERIC].
1.5 mg (Rx) [Cortalone; Triacet; Triamtabs; GENERIC].
Canada—
Veterinary-labeled product(s): Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F) in a well-closed container, unless otherwise specified by the manufacturer.

USP requirements: Preserve in well-closed containers. Contain the labeled amount, within ±10%. Meet the requirements for Identification, Dissolution (75% in 45 minutes in water in Apparatus 2 at 50 rpm), and Uniformity of dosage units.{R-110}

TRIAMCINOLONE ACETONIDE INJECTABLE SUSPENSION USP
Usual dose:

{R-15}Allergic disorders{R-21}; or
{R-16}Dermatoses{R-21}—Cats and dogs: Intramuscular or subcutaneous, 0.11 to 0.22 mg per kg of body weight as a single dose.{R-22} If symptoms recur, the dose may be repeated after seven to fifteen days.{R-22}

Note: For dermatitis, 0.22 mg per kg as a single dose is recommended.{R-22}

For injections directly into the lesion, a total dose of 1.2 to 1.8 mg as a single dose is used.{R-22} It is recommended that the dose at any one site should not exceed 0.6 mg and should be made well into the cutis. Injections are circumscribed around the lesion using a tuberculin syringe with a small bore needle (23 to 25 gauge). When multiple lesions are treated, the total dose should not exceed 6 mg.{R-22}

{R-16}Inflammation{R-21}, including musculoskeletal inflammation—
Cats and dogs: Intramuscular or subcutaneous, 0.11 to 0.22 mg per kg of body weight as a single dose.{R-22} If symptoms recur, the dose may be repeated after seven to fifteen days.{R-22}

Horses: Intramuscular or subcutaneous, 0.022 to 0.044 mg per kg of body weight as a single dose.{R-22}
Withdrawal times: U.S.—Triamcinolone acetonide suspension is not labeled for use in horses intended for food.{R-22}

Inflammation, musculoskeletal (joint)—
Cats and dogs: Intra-articular or intrasynovial, a total dose of 1 to 3 mg as a single dose.{R-21} The dose may be repeated after three to four days, if necessary.{R-22}

Horses: Intra-articular or intrasynovial, 6 to 18 mg as a total single dose.{R-21} The dose may be repeated after three to four days, if necessary.{R-22}
Withdrawal times: U.S.—Triamcinolone acetonide suspension is not labeled for use in horses intended for food.{R-22}

Note: If marked increases in pain, local swelling, restriction of joint motion, and fever are noted, septic arthritis should be considered. If sepsis is present, antimicrobial therapy should be instituted immediately.{R-22}

Parturition induction{R-25}—Pretreatment dose: Cattle—Intramuscular, 0.016 mg per kg of body weight, given one week before induction of parturition with dexamethasone.

Note: Forty percent of cows given this pretreatment may calve before the parturition induction dose that is administered 6 days later.{R-110}

Note: {R-15}Chronic obstructive pulmonary disease{R-21}—Horses: Although the safety and efficacy have not been established in the treatment of chronic obstructive pulmonary disease in horses, a single intramuscular dose of 0.09 mg per kg of body weight may be effective in the relief of signs for up to four weeks.{R-110}

Strength(s) usually available:{R-14}
U.S.—
Veterinary-labeled product(s){R-24}
2 mg per mL (Rx) [Vetalog] .
6 mg per mL (Rx) [Vetalog].
Canada—
Veterinary-labeled product(s): Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by the manufacturer. Protect from freezing.{R-22}

USP requirements: Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light. A sterile suspension of Triamcinolone Acetonide in a suitable aqueous medium. Contains the labeled amount, within ~10% to +15%. Meets the requirements for Identification, Bacterial
References

1. Panel comment, Rec 4/14/98.
11. Danexamethasone sodium phosphate injection package insert (Generic, Vedco—US), Rev 12/01, Rec 8/6/03.
32. Personal communication with Dr Hoc, 5/26/98.


110. Kords E, Jochle W. Induced parturition in dairy cattle: a comparison of a corticoid (flumethasone) and a prostaglandin (PGF2alpha) in different age groups. Theriogenology 1975 May; 3(5): 171-8.
122. Panel comment, Rec 4/13/98.


177. Reviewer comment, 10/4/96.