

## CORTICOSTEROIDS—GLUCOCORTICOID EFFECTS (Veterinary—Systemic)

This monograph contains information on the following: Dexamethasone; Flumethasone; Hydrocortisone; Isoflupredone; Methylprednisolone; Prednisolone; Prednisone; Triamcinolone.

Some commonly used *brand names* are:

For veterinary-labeled products—

<i>Azium Powder</i> [Dexamethasone]	<i>Medrol</i> [Methylprednisolone]
<i>Azium Solution</i> [Dexamethasone]	<i>Methysone 40</i> [Methylprednisolone]
<i>Cortalone</i> [Triamcinolone]	<i>Predef 2X</i> [Isoflupredone]
<i>Depo-Medrol</i> [Methylprednisolone]	<i>PrednisTab</i> [Prednisolone]
<i>Dexaject</i> [Dexamethasone]	<i>Predsonex-5</i> [Prednisone]
<i>Dexaject SP</i> [Dexamethasone]	<i>Rafter Dex</i> [Dexamethasone]
<i>Dexamethasone 2</i> [Dexamethasone]	<i>Solu-Delta-Cortef</i> [Prednisolone]
<i>Dexamethasone 5</i> [Dexamethasone]	<i>Triamtabs</i> [Triamcinolone]
<i>Dexasone</i> [Dexamethasone]	<i>Uni-Dex</i> [Dexamethasone]
<i>Dexazone 2 mg</i> [Dexamethasone]	<i>Unimed</i> [Methylprednisolone]
<i>Dexium</i> [Dexamethasone]	<i>Uni-Pred 50</i> [Prednisolone]
<i>Dexone</i> [Dexamethasone]	<i>Vetacortyl</i> [Methylprednisolone]
<i>Dextab</i> [Dexamethasone]	<i>Vetalog</i> [Triamcinolone]
<i>Flucort</i> [Flumethasone]	

For human-labeled products—

<i>A-methaPred</i> [Methylprednisolone]	<i>Hexadrol</i> [Dexamethasone]
<i>Cortef</i> [Hydrocortisone]	<i>Hydrocortone</i> [Hydrocortisone]
<i>Decadron</i> [Dexamethasone]	<i>Solu-Medrol</i> [Methylprednisolone]
<i>Dexasone</i> [Dexamethasone]	

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; Isoflupredone; Methylprednisolone; Prednisolone; Prednisone; Triamcinolone.
- Diagnostic aid (hyperadrenocorticism)—Dexamethasone.
- Gluconeogenic agent—Dexamethasone; Flumethasone; Isoflupredone; Prednisolone.
- Immunosuppressant—Prednisolone; Prednisone.
- Parturifacient—Dexamethasone; Flumethasone.

### Indications

Note: Bracketed information in the *Indications* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

Information identified by a superscript 1 refers to uses that either are not included in Canadian product labeling or are for products not commercially available in Canada.

### General considerations

Glucocorticoids potentially affect every cell in the body and produce a wide spectrum of effects depending on tissue concentration and cell type.<sup>[R-30]</sup> 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.<sup>{R-18; 23}</sup> 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.<sup>{R-4; 6; 8; 11; 12; 14; 16; 17; 20; 22}</sup> For clarity, specific indications noted on product labeling are listed in this section as unbracketed *Accepted* indications and those not specifically named in U.S. or Canadian labeling are bracketed or marked with a superscript 1, 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<sup>{R-34; 145}</sup> 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<sup>{R-8}</sup> 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.<sup>{R-213}</sup> Relative mineralocorticoid effect from the most to the least potency is hydrocortisone > prednisolone/prednisone > methylprednisolone > dexamethasone.<sup>{R-38; 188}</sup>

**Cats:** Methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> [hydrocortisone tablets]<sup>1</sup>,<sup>{R-193}</sup> prednisolone sodium succinate injection, [prednisolone tablets]<sup>1</sup>,<sup>{R-193}</sup> and [prednisone tablets]<sup>1</sup><sup>{R-193}</sup> are indicated in the treatment of acute adrenocortical insufficiency.

**Dogs:** Prednisolone sodium succinate<sup>{R-7; 9}</sup> is indicated in the treatment of acute adrenocortical insufficiency when a rapid effect is necessary. Methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> prednisolone tablets<sup>1</sup>,<sup>{R-8}</sup> [hydrocortisone tablets]<sup>1</sup>,<sup>{R-193}</sup> and [prednisone tablets]<sup>1</sup><sup>{R-100; 195}</sup> are also indicated in the treatment of acute adrenocortical insufficiency.

**Horses:** Dexamethasone sodium phosphate<sup>{R-11}</sup> is indicated for use in situations in which a rapid adrenocortical effect is needed; however, it provides no significant mineralocorticoid effect. [Prednisolone]<sup>1</sup> and [prednisone]<sup>1</sup> have been used in the treatment of adrenocortical insufficiency.

**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,<sup>{R-15; 16}</sup> methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> triamcinolone acetonide injectable suspension<sup>1</sup>,<sup>{R-22}</sup> and triamcinolone tablets<sup>1</sup><sup>{R-20}</sup> are indicated in the treatment of allergic conditions. [Flumethasone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of allergic disorders.<sup>{R-100; 194}</sup>

*Cattle*: Isoflupredone acetate injectable suspension<sup>{R-23; 24}</sup> and dexamethasone injection<sup>{6}</sup> are indicated in the treatment of allergic conditions. Although they are not labeled for use in cattle in the U.S., [flumethasone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of allergic disorders.

*Dogs*: Dexamethasone injection, flumethasone injection<sup>{R-18}</sup>, methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets<sup>1, {R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> prednisolone tablets<sup>1, {R-8}</sup> triamcinolone acetonide injectable suspension<sup>1, {R-22}</sup> and triamcinolone tablets<sup>1, {R-20}</sup> are indicated in the treatment of allergic conditions. [Prednisone]<sup>1</sup> should also be effective in the treatment of allergic disorders.<sup>{R-100}</sup>

*Horses*: Dexamethasone injection, flumethasone injection<sup>1, {R-18}</sup> isoflupredone acetate injectable suspension,<sup>{R-23; 24}</sup> and prednisolone sodium succinate<sup>{R-7; 9}</sup> are indicated in the treatment of allergic conditions. [Methylprednisolone]<sup>1</sup> and [prednisone]<sup>1</sup> should also be effective in the treatment of allergic disorders.<sup>{R-100; 194}</sup>

*Pigs*: Isoflupredone acetate injectable suspension<sup>{R-23; 24}</sup> is indicated in the treatment of allergic conditions. Although they are not labeled for use in pigs, [dexamethasone]<sup>1</sup>, [flumethasone]<sup>1</sup>, [methylprednisolone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of allergic disorders.

*Asthma, bronchial (treatment)—Cats*: Methylprednisolone acetate injection or tablets<sup>1, {R-14; 192}</sup> [prednisolone]<sup>1, {R-100; 193}</sup> or [prednisone tablets]<sup>{R-28; 100; 193}</sup> are indicated in the treatment of bronchial asthma. 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.<sup>{R-213}</sup>

*Colitis, ulcerative (treatment)—Dogs*: Methylprednisolone tablets,<sup>{R-14; 192}</sup> prednisolone tablets,<sup>{R-8}</sup> and [prednisone]<sup>{R-100}</sup> are indicated in the treatment of ulcerative colitis in dogs; however, use typically is reserved for cases that are not responsive to other therapies.

Dermatitis, allergic (treatment);

Dermatoses, nonallergic (treatment);

Otitis (treatment); or

*Pruritus (treatment)—Once initial inflammation is controlled, other methods of controlling disease should be pursued. If corticosteroid treatment must be continued, the lowest dose necessary or, if possible, alternate day therapy with either prednisolone, prednisone, methylprednisolone, or triamcinolone should be instituted.<sup>{R-213}</sup> Repeated injections of acetate or acetonide repository injections are not recommended for control of chronic skin disease because of the risk of iatrogenic hyperadrenocorticism.*

*Cats*: Dexamethasone injection,<sup>{R-4}</sup> [dexamethasone tablets],<sup>{R-12}</sup> flumethasone injection,<sup>{R-18}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets<sup>1, {R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-9}</sup> [prednisolone tablets]<sup>1</sup>, [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1, {R-22}</sup> and triamcinolone tablets<sup>1, {R-20}</sup> are indicated in the treatment of acute and chronic dermatoses of varying etiologies and the associated inflammation, irritation, and pruritus. Methylprednisolone tablets<sup>1, {R-14; 192}</sup> are labeled for the treatment of otitis externa.

*Dogs*: Dexamethasone injection,<sup>{R-4}</sup> [dexamethasone tablets],<sup>{R-12}</sup> flumethasone injection,<sup>{R-18}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets<sup>1, {R-14; 192}</sup> [prednisolone acetate injectable suspension],<sup>{R-10}</sup> prednisolone sodium succinate,<sup>{R-9}</sup> prednisolone tablets<sup>1, {R-8}</sup> [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1, {R-22}</sup> and triamcinolone tablets<sup>1, {R-20}</sup> are indicated in the treatment of acute and chronic dermatoses of varying etiologies and the associated inflammation, irritation, and pruritus. Flumethasone injection,<sup>{R-18}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets<sup>1, {R-14; 192}</sup> and prednisolone tablets<sup>1, {R-8}</sup> are labeled for the treatment of otitis externa.

Disk disease, intervertebral (treatment)—*Dogs*: Dexamethasone injection<sup>{R-4}</sup> and flumethasone injection<sup>{R-18}</sup> are indicated as supportive therapy in the treatment of intervertebral disk disease (disk syndrome). But it should be noted that high dosages of dexamethasone carry a risk of severe adverse effects.<sup>{R-166}</sup> Therapy should be tailored to the type of disk dysfunction and clinical signs. [Methylprednisolone]<sup>1</sup>, [prednisolone]<sup>1</sup>, or [prednisone]<sup>1</sup>, administered at an anti-inflammatory dosage, may be a more appropriate choice of therapy in many cases. 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, general (treatment)—

*Cats*: Dexamethasone injection,<sup>{R-4; 181}</sup> [dexamethasone sodium phosphate injection],<sup>{R-176}</sup> dexamethasone tablets,<sup>{R-12}</sup> [flumethasone injection],<sup>{R-18; 185}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets,<sup>1 {R-14}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> [prednisolone tablets]<sup>1</sup>, [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1 {R-22}</sup> and triamcinolone tablets<sup>1 {R-20}</sup> are indicated in the treatment of inflammation known to be responsive to glucocorticoids.

*Cattle*: Dexamethasone injection,<sup>{R-4; 6; 176; 181}</sup> dexamethasone oral powder,<sup>{R-3; 5}</sup> [dexamethasone sodium phosphate injection],<sup>{R-176}</sup> and [flumethasone injection]<sup>{R-185}</sup> are indicated in the treatment of inflammation known to be responsive to glucocorticoids. Although they are not labeled for use in cattle in the U.S., [prednisolone]<sup>1</sup> and [prednisone]<sup>1</sup> should also be effective in the treatment of general inflammation.

*Dogs*: Dexamethasone injection,<sup>{R-181}</sup> dexamethasone sodium phosphate injection,<sup>{R-176}</sup> dexamethasone tablets,<sup>{R-12}</sup> flumethasone injection,<sup>{R-18; 185}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets,<sup>1 {R-14}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> prednisolone tablets,<sup>1 {R-8}</sup> [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1 {R-22}</sup> and triamcinolone tablets<sup>1 {R-20}</sup> are indicated in the treatment of inflammation known to be responsive to glucocorticoids.

*Horses*: Dexamethasone injection,<sup>{R-4; 6; 11; 176; 181}</sup> dexamethasone sodium phosphate injection, dexamethasone oral powder,<sup>{R-5}</sup> flumethasone injection,<sup>{R-18; 185}</sup> methylprednisolone acetate injectable suspension,<sup>1 {R-15; 16; 17}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> and triamcinolone acetonide injectable suspension<sup>1 {R-22}</sup> are indicated in the treatment of inflammation known to be responsive to glucocorticoids.

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 present.

*Cats*: Dexamethasone injection,<sup>{R-4}</sup> [dexamethasone tablets],<sup>{R-12}</sup> [flumethasone injection], methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets,<sup>1 {R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-9}</sup> [prednisolone tablets]<sup>1 {R-28; 31; 189}</sup> [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1 {R-22}</sup> and triamcinolone tablets<sup>1 {R-20}</sup> are indicated in the treatment of joint and musculoskeletal inflammation. Intra-articular administration of triamcinolone injectable suspension<sup>1 {R-22}</sup> is indicated in the treatment of joint inflammation; however, the risk of local adverse effects, including postinjection flare-up and septic arthritis, is increased, particularly with repeated injections. There is some concern that high dose regimens may cause articular surface damage.<sup>{R-197}</sup> Use of the lowest dose at the longest dosing interval possible is recommended if intra-articular injection is necessary.<sup>{R-197}</sup>

*Cattle*: Dexamethasone injection,<sup>{R-4}</sup> dexamethasone oral powder,<sup>{R-5}</sup> [dexamethasone 21 phosphate injection],<sup>{R-1}</sup> [flumethasone injection],<sup>{R-185}</sup> and isoflupredone acetate injectable suspension<sup>{R-23; 24}</sup> are indicated in the treatment of joint and musculoskeletal inflammation. Although they are not labeled for use in cattle in

the U.S., [prednisolone]<sup>1</sup> and [prednisone]<sup>1</sup> should also be effective in the treatment of musculoskeletal inflammation.

*Dogs:* Dexamethasone injection,<sup>{R-4}</sup> [dexamethasone tablets],<sup>{R-12}</sup> flumethasone injection,<sup>{R-18}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> [prednisolone acetate injectable suspension],<sup>{R-10}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> prednisolone tablets<sup>1</sup>,<sup>{R-8}</sup> [prednisone tablets],<sup>{R-28}</sup> triamcinolone acetonide injectable suspension<sup>1</sup>,<sup>{R-22}</sup> and triamcinolone tablets<sup>1</sup>,<sup>{R-20}</sup> are indicated in the treatment of joint and musculoskeletal inflammation, including arthritis,<sup>{R-17; 99}</sup> bursitis,<sup>{R-14; 192}</sup> myositis,<sup>{R-14; 192}</sup> and osteoarthritis.<sup>{R-17}</sup>

Intra-articular administration of flumethasone injection,<sup>{R-18}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> and triamcinolone acetonide injectable suspension<sup>1</sup>,<sup>{R-22}</sup> are indicated in the treatment of joint inflammation; however, the risk of local adverse effects, including postinjection flare-up and septic arthritis, is increased, particularly with repeated injections, and there is some concern that high dose regimens may cause articular surface damage.<sup>{R-197}</sup> Use of the lowest dose at the longest dosing interval possible is recommended if intra-articular injection is necessary.<sup>{R-197}</sup>

*Horses:* Dexamethasone injection,<sup>{R-4; 176}</sup> dexamethasone oral powder,<sup>{R-5}</sup> [dexamethasone 21 phosphate injection],<sup>{R-1}</sup> flumethasone injection,<sup>{R-18}</sup> isoflupredone acetate injectable suspension,<sup>{R-23; 24}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> [prednisolone acetate injectable suspension],<sup>{R-10}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> and triamcinolone acetonide injectable suspension<sup>1</sup>,<sup>{R-22}</sup> are indicated in the treatment of joint and musculoskeletal inflammation, including bursitis,<sup>{R-6; 16}</sup> carpalis,<sup>{R-6; 16}</sup> osselets,<sup>{R-6; 16}</sup> myositis,<sup>{R-6; 16}</sup> osteoarthritis,<sup>{R-16; 17}</sup> periostitis,<sup>{R-16; 17}</sup> sprains,<sup>{R-6; 16}</sup> synovitis,<sup>{R-16; 17}</sup> or tenosynovitis.<sup>{R-16; 17}</sup>

Intra-articular administration of flumethasone injection,<sup>{R-18}</sup> isoflupredone acetate injectable suspension,<sup>{R-23; 24}</sup> methylprednisolone acetate injectable suspension,<sup>{R-15; 16; 17}</sup> or triamcinolone acetonide injectable suspension<sup>1</sup>,<sup>{R-22}</sup> is indicated in the treatment of joint inflammation to avoid the systemic side effects of these medications,<sup>{R-122}</sup> however, joint tissue repair is delayed,<sup>{R-122}</sup> some systemic absorption and adrenal suppression occurs,<sup>{R-121; 129}</sup> and the risk of local adverse effects, including postinjection flare up and septic arthritis,<sup>{R-121}</sup> is increased, particularly with repeated injections.<sup>{R-121-126}</sup> Intra-articular glucocorticoids, such as methylprednisolone, also can mask the clinical signs of infectious arthritis for up to 3 days.<sup>{R-128}</sup> Use of the lowest dose at the longest dosing interval possible is recommended if intra-articular injection is necessary.<sup>{R-197}</sup>

*Pigs:* Isoflupredone acetate injectable suspension<sup>1</sup>,<sup>{R-23}</sup> is indicated in the treatment of joint and musculoskeletal inflammation. Although they are not labeled for use in pigs, [dexamethasone]<sup>1</sup>, [flumethasone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of musculoskeletal inflammation.

#### Inflammation, ocular (treatment)—

*Cats:* Methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> [prednisolone tablets]<sup>1</sup>, and [prednisone tablets]<sup>1</sup>,<sup>{R-193}</sup> are indicated in the treatment of inflammatory conditions of the eye, including chorioretinitis, secondary glaucoma, iriditis, iridocyclitis, and uveitis. [Dexamethasone]<sup>1</sup> and [flumethasone]<sup>1</sup> should also be effective in the treatment of ocular inflammation.

*Cattle:* Isoflupredone acetate injectable suspension<sup>1</sup>,<sup>{R-23}</sup> and [dexamethasone injection]<sup>1</sup> are indicated in the treatment of inflammatory conditions of the eye. Although not labeled for use in cattle in the U.S., [flumethasone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of ocular inflammation.

*Dogs:* Methylprednisolone tablets<sup>1</sup>,<sup>{R-14; 192}</sup> prednisolone sodium succinate,<sup>{R-7; 9}</sup> prednisolone tablets<sup>1</sup>,<sup>{R-8}</sup> and [prednisone tablets]<sup>1</sup>,<sup>{R-100}</sup> are indicated in the treatment of inflammatory conditions of the eye, including chorioretinitis, secondary

glaucoma, iriditis, iridocyclitis, and uveitis. [Dexamethasone]<sup>1</sup> and [flumethasone]<sup>1</sup> should also be effective in the treatment of ocular inflammation.

*Horses:* Isoflupredone acetate injectable suspension<sup>(R-23)</sup> and prednisolone sodium succinate<sup>(R-7; 9)</sup> are indicated in the treatment of inflammatory conditions of the eye. [Dexamethasone]<sup>1</sup>, [flumethasone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of ocular inflammation.

*Pigs:* Isoflupredone acetate injectable suspension<sup>(R-23)</sup> is indicated in the treatment of inflammatory conditions of the eye. Although not labeled for use in pigs in the U.S., [dexamethasone]<sup>1</sup>, [flumethasone]<sup>1</sup>, [prednisolone]<sup>1</sup>, and [prednisone]<sup>1</sup> should also be effective in the treatment of ocular inflammation.

**Ketosis (treatment)—Cattle:** Dexamethasone injection,<sup>(R-4; 6)</sup> [dexamethasone 21 phosphate injection],<sup>(R-1)</sup> [dexamethasone sodium phosphate injection],<sup>(R-176)</sup> dexamethasone oral powder,<sup>(R-5)</sup> [flumethasone injection],<sup>(R-185)</sup> isoflupredone acetate injectable suspension,<sup>(R-23)</sup> and [prednisolone acetate injectable suspension]<sup>(R-10)</sup> are indicated in the treatment of primary bovine ketosis and are likely to be more effective when administered with intravenous glucose solutions.<sup>(R-57)</sup> For secondary bovine ketosis, corticosteroids should be used concurrently with other therapies for underlying disease, including local and systemic antibacterials to treat primary bacterial infections.<sup>(R-23)</sup> A significant decrease in milk production should be expected when a corticosteroid is administered to lactating cattle.<sup>(R-213)</sup>

**Shock, septic (treatment adjunct)—**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,<sup>(R-47)</sup> a wide variety of research has been done, often with contradictory results.<sup>(R-47-52)</sup> 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.<sup>(R-47-50)</sup> Because studies have shown flunixin to be at least as effective as or superior to glucocorticoids in the treatment of endotoxemia in calves and ponies<sup>(R-47-51)</sup> without the risk of attenuation of immune defenses, its use may be preferred in some situations.

*Cats:* Methylprednisolone acetate injectable suspension is indicated in the treatment of septic shock,<sup>(R-15; 16)</sup> however, the rapid-acting corticosteroid formulations, such as [dexamethasone sodium phosphate]<sup>1</sup> and prednisolone sodium succinate,<sup>(R-7; 9)</sup> 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,<sup>(R-15; 16)</sup> however, the rapid-acting corticosteroid formulations, such as [dexamethasone sodium phosphate]<sup>1</sup> and prednisolone sodium succinate,<sup>(R-7; 9)</sup> 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,<sup>(R-23)</sup> however, the rapidly acting corticosteroid formulations, such as [dexamethasone sodium phosphate]<sup>1</sup>, 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,<sup>(R-23)</sup> however, the rapid-acting corticosteroid formulations, such as [dexamethasone sodium phosphate]<sup>1</sup> and prednisolone sodium succinate,<sup>(R-7; 9)</sup> 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]<sup>1</sup>—*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.<sup>{R-190; 191}</sup> Although it is usually administered in conjunction with a prostaglandin, there is still a risk of fetal mummification, retained placentas, metritis, or dystocia.<sup>{R-191}</sup> It should be noted that abortion can be associated with any C16-methylated glucocorticoid (see the *Side/Adverse Effects* section).<sup>{R-213}</sup>

[Anemia, immune-mediated hemolytic (treatment)]<sup>1</sup>—*Cats and dogs*: Dexamethasone, prednisolone, and prednisone are used in the treatment of autoimmune hemolytic anemia.<sup>{R-96; 100; 106}</sup> Primary underlying causes should be ruled out to be certain therapy is appropriate. Glucocorticoids may be used in conjunction with other immunosuppressive drugs. In the treatment of some anemia cases, medications may be used in conjunction with blood transfusion or splenectomy.<sup>{R-96; 106}</sup>

[Hyperadrenocorticism (diagnosis)]<sup>1</sup>—

*Cats*: Dexamethasone injection and dexamethasone sodium phosphate injection are used in the diagnosis of hyperadrenocorticism (Cushing's syndrome).<sup>{R-140}</sup> Because of the lack of consistent clinical signs in cats to support a diagnosis of hyperadrenocorticism and, therefore, the small number of recognized cases available for testing, tests are used for diagnosis based on studies performed with normal cats.<sup>{R-140; 222}</sup> The screening test is generally performed with a dose higher than that used in the low-dose test for dogs; the high dose is more than 90% diagnostic for normal cats.<sup>{R-140}</sup> Differentiation of adrenal disease versus pituitary-dependent hyperadrenocorticism has been performed by some clinicians<sup>{R-221}</sup> with a higher dose than that used for the high-dose dexamethasone test in dogs; however, there is no substantive research evidence to show that the two can be differentiated by this test in cats.<sup>{R-177}</sup>

*Dogs*: Dexamethasone injection and dexamethasone sodium phosphate injection are used in the diagnosis of hyperadrenocorticism (Cushing's syndrome).<sup>{R-58; 62-64}</sup> The low-dose dexamethasone test typically is 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<sup>{R-60; 62}</sup> in screening for hyperadrenocorticism and possibly 61% accurate in differentiation of pituitary- from adrenal-disease.<sup>{R-64}</sup> The high-dose dexamethasone test is 75 to 80% accurate in differentiating the two forms of this disorder.<sup>{R-63; 64}</sup>

*Horses*: Dexamethasone injection is used in the diagnosis of pituitary pars intermedia-dependent hyperadrenocorticism.<sup>{R-178; 179}</sup>

[Lupus erythematosus, systemic (treatment)]<sup>1</sup>—*Dogs*:

Methylprednisolone, prednisolone, and prednisone are used in the treatment of systemic lupus erythematosus.<sup>{R-98; 99}</sup>

[Lymphoma (treatment adjunct)]<sup>1</sup>—*Cats and dogs*: Prednisolone and prednisone are used in the treatment of lymphoma.<sup>{R-83-89; 100; 109}</sup>

Although prednisone alone can cause some remission of signs,<sup>{R-86; 87}</sup> tumor resistance develops quickly and remission is short;<sup>{R-86}</sup> therefore, corticosteroids are more commonly used in combination chemotherapy with other agents. One widely used combination protocol includes prednisone, cyclophosphamide, and vincristine (COP), although there are many published regimens.<sup>{R-86; 90}</sup> Treatment with corticosteroids alone can decrease the chance of remission with combination therapies instituted later,<sup>{R-83}</sup> however, prednisone has been used as a single therapy when cost or other factors warrant it.<sup>{R-109}</sup>

[Mast cell tumors (treatment)]<sup>1</sup>—*Dogs*: Prednisolone<sup>{R-100}</sup> and prednisone<sup>{R-107; 108}</sup> are used in the treatment of mast cell tumors, although initial wide surgical excision, if possible, is generally the primary treatment. In a group of dogs with relatively aggressive tumors (grades II and III), prednisone was shown to be effective in reducing tumor size in 20% of cases.<sup>{R-107}</sup>

[Parturition, induction of]<sup>1</sup>—

*Cattle*: Dexamethasone and flumethasone have been used in the induction of parturition,<sup>{R-110-113}</sup> 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.<sup>(R-111; 113)</sup> Administration of corticosteroids more than 1 month before expected gestation often leads to poor neonatal survival<sup>(R-114)</sup> 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 in order to produce a predictable response time.<sup>(R-110)</sup> 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);<sup>(R-110; 112; 114)</sup> however, in 40% of cows, the triamcinolone preadministration 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;<sup>(R-116; 117)</sup> however, these products are not labeled for use in sheep in the U.S.

[Pemphigoid (treatment)]<sup>1</sup>; or

[Pemphigus (treatment)]<sup>1</sup>—*Cats and dogs:* Prednisolone<sup>(R-40; 41)</sup> and prednisone<sup>(R-39; 42)</sup> 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.<sup>(R-39-42)</sup>

[Spinal cord trauma, acute (treatment)]<sup>1</sup>—*Cats and dogs:*

Methylprednisolone sodium succinate has been shown to improve clinical outcome in cats when administered within 1 hour of acute experimental spinal cord trauma.<sup>(R-25; 44; 45; 91; 173; 182)</sup> The strength of evidence of efficacy of methylprednisolone sodium succinate in cats leads clinicians to recommend use for this indication in dogs, also.

[Thrombocytopenia, immune-mediated (treatment)]<sup>1</sup>—*Dogs:*

Prednisolone<sup>(R-94-96)</sup> and prednisone<sup>(R-100)</sup> are used in the treatment of immune-mediated thrombocytopenia.<sup>(R-94-96)</sup> Other underlying causes of thrombocytopenia, such as infection, drug reactions, or neoplasia, should be ruled out to be certain therapy is appropriate.<sup>(R-94; 95)</sup> In cases that are initially refractory to prednisolone, other immunosuppressive medications, such as vincristine or cyclophosphamide, may be added.<sup>(R-94)</sup>

### Acceptance not established

Note: Product labeling in the U.S. and Canada includes the use of glucocorticoids<sup>(R-4; 5; 23; 24)</sup> 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)<sup>1</sup>—*Cats and dogs:* Although the use of prednisolone in the treatment of glomerular disease (nephrosis) is mentioned on U.S. product labeling,<sup>(R-8)</sup> the efficacy and safety of this use has not been established and is not recommended.<sup>(R-194)</sup> 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.<sup>(R-174)</sup> 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.<sup>(R-175)</sup> The use of corticosteroids in the treatment of immune-mediated



glomerulonephritis is not recommended.

Mastitis (treatment)<sup>1</sup>—*Cattle*: Although some product labeling mentions the use of dexamethasone as supportive therapy in the treatment of mastitis,<sup>{R-4}</sup> 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*<sup>{R-142; 143; 144}</sup> 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.<sup>{R-143; 144}</sup> 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.<sup>{R-142}</sup> Glucocorticoid therapy cannot be used in pregnant cows in middle- to late-gestation without risk of induction of abortion or parturition.<sup>{R-110-114; 142}</sup>

[Abortion, induction of]<sup>1</sup>—

*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.<sup>{R-118}</sup> Frequent oral dosing for 10 days resulted in abortion in all treated dogs,<sup>{R-118}</sup> 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.<sup>{R-172}</sup> Dexamethasone is not labeled for use in sheep in the U.S. or Canada.

[Anemia, immune-mediated hemolytic (treatment)]<sup>1</sup>—*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.<sup>{R-97}</sup>

[Chronic obstructive pulmonary disease (treatment)]<sup>1</sup>—*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.<sup>{R-32; 100; 199; 200}</sup> Research studies are limited and give conflicting results on efficacy, perhaps due to variable severity of the disease and problems with diagnosis and evaluation.<sup>{R-199; 200}</sup> Efforts to decrease environmental irritants are very important in the control of this disorder;<sup>{R-201}</sup> bronchodilators are also often part of the therapeutic strategy.<sup>{R-32}</sup> The risk of side effects, such as adrenal suppression and, possibly, laminitis, with chronic systemic administration of corticosteroids to horses should be considered.<sup>{R-202}</sup>

[Inflammation, neurologic (treatment)]<sup>1</sup>—*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.<sup>{R-30; 43}</sup> 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 flumethasone injection,<sup>{R-4; 18}</sup> 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.<sup>{R-44; 91; 92}</sup> Dexamethasone has been shown to decrease significantly the edema associated with induced brain tumors<sup>{R-219}</sup> but to have little effect on edema associated with induced trauma to the brain,<sup>{R-220}</sup> however, there is some evidence that methylprednisolone can improve recovery from neurologic dysfunction associated with brain trauma.<sup>{R-93}</sup> 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.<sup>{R-44; 45}</sup>

Glucocorticoids typically are used as adjunctive therapy in acute, subacute, and chronic neurological 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.<sup>{R-141}</sup>

[Inflammatory bowel disease (treatment)]<sup>1</sup>—*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.<sup>{R-198}</sup> 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.<sup>{R-193}</sup> Therapies such as diet control may be instituted in conjunction with a medication or a combination of medications.<sup>{R-198}</sup>

[Respiratory distress syndrome (treatment)]<sup>1</sup>—*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.<sup>{R-217}</sup> Dexamethasone and flumethasone have been shown to increase pulmonary surfactant in various species,<sup>{R-217; 218}</sup> however, only dexamethasone is labeled for use in food-producing animals in the U.S.

[Shock, cardiogenic (treatment adjunct)]<sup>1</sup>; or  
[Shock, hemorrhagic (treatment adjunct)]<sup>1</sup>—*All species*: Although U.S. and Canadian product labeling includes the use of glucocorticoids in the treatment of shock, there are insufficient data to confirm the safety and efficacy of this use in cardiogenic or hemorrhagic shock. Canadian product labeling for dexamethasone injection includes use as an adjunct in the treatment of shock in cats, dogs, and horses.<sup>{R-184}</sup> In the U.S. and Canada, isoflupredone acetate injectable suspension is labeled for the treatment of shock in cattle, horses, and pigs.<sup>{R-23}</sup> flumethasone injection is labeled for the treatment of shock in dogs.<sup>{R-18}</sup>

The use of glucocorticoids in the treatment of cardiogenic and hemorrhagic shock continues in the face of conflicting research data.<sup>{R-53-56}</sup> The primary treatment of shock is the administration of large volumes of crystalloid solutions.<sup>{R-56}</sup> High doses of glucocorticoids may aid in reversing some of the effects of shock when administered in conjunction with intravenous fluids.<sup>{R-54-56}</sup> 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.<sup>{R-213}</sup> These rapidly acting medications include dexamethasone sodium phosphate and prednisolone sodium succinate.

### Unaccepted

Laminitis, acute (treatment)—*Horses*: Although product labeling for dexamethasone<sup>{R-4}</sup> and prednisolone sodium succinate<sup>{R-7}</sup> 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.<sup>{R-212}</sup> The venom transmitted in a poisonous snakebite will vary depending on the species and condition of the snake.<sup>{R-180}</sup> 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.<sup>{R-212}</sup> 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.

[Appetite, lack of (treatment)]—*Cats*: Although Canadian product labeling includes the use of flumethasone injection in the stimulation of appetite in cats,<sup>{R-185}</sup> clinical use does not suggest that debilitated animals experience an increase in appetite with corticosteroid administration.<sup>{R-194}</sup> Other medications, such as cyproheptadine or a benzodiazepine, are more accepted choices for this indication.<sup>{R-212}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Regulatory Considerations

U.S.—

Dexamethasone oral powder, 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 21 phosphate, 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.<sup>{R-31}</sup>

Dexamethasone—A synthetic analog of prednisolone.<sup>{R-6}</sup>

Flumethasone—A chemical modification of prednisolone.<sup>{R-18}</sup>

Methylprednisolone—A 6-methyl derivative of prednisolone.<sup>{R-14; 192}</sup>

Prednisolone—A synthetic dehydrogenated analogue of cortisone.<sup>{R-8}</sup>

### Chemical name:

Dexamethasone—Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11 beta,16 alpha)-.<sup>{R-29}</sup>

Dexamethasone sodium phosphate—Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonoxy)-, disodium salt, (11 beta,16 alpha)-.<sup>{R-29}</sup>

Hydrocortisone—Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11 beta)-.<sup>{R-29}</sup>

Isoflupredone acetate—Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-, (11 beta)-.<sup>{R-29}</sup>

Methylprednisolone—Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-6-methyl-, (6 alpha,11 beta)-.<sup>{R-29}</sup>

Methylprednisolone acetate—Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-6-methyl-, (6 alpha,11 beta)-.<sup>{R-29}</sup>

Methylprednisolone sodium succinate—Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, monosodium salt, (6 alpha,11 beta)-.<sup>{R-29}</sup>

Prednisolone—Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-, (11 beta)-.<sup>{R-29}</sup>

Prednisolone acetate—Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-, (11 beta)-.<sup>{R-29}</sup>

Prednisolone sodium succinate—Pregna-1,4-diene-3,20-dione, 21-(3-carboxyl-1-oxopropoxy)-11,17-dihydroxy-, monosodium salt, (11 beta)-.<sup>{R-29}</sup>

Prednisone—Pregna-1,4-diene-3,11,20-trione monohydrate, 17,21-dihydroxy-.<sup>{R-29}</sup>

Triamcinolone—Pregna-1,4-diene-3,20-dione, 9-fluoro-11,16,17,21-tetrahydroxy-, (11 beta,16 alpha)-.<sup>{R-29}</sup>

Triamcinolone acetonide—Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis-(oxy)]-, (11 beta,16 alpha)-.<sup>{R-29}</sup>

### Molecular formula:

Dexamethasone—C<sub>22</sub>H<sub>29</sub>FO<sub>5</sub>.<sup>{R-29}</sup>

Dexamethasone sodium phosphate—C<sub>22</sub>H<sub>28</sub>FNa<sub>2</sub>O<sub>8</sub>P.<sup>{R-29}</sup>

Hydrocortisone—C<sub>21</sub>H<sub>30</sub>O<sub>5</sub>.<sup>{R-29}</sup>

Isoflupredone acetate— $C_{23}H_{29}FO_6$ .<sup>{R-29}</sup>  
Methylprednisolone— $C_{22}H_{30}O_5$ .<sup>{R-29}</sup>  
Methylprednisolone acetate— $C_{24}H_{32}O_6$ .<sup>{R-29}</sup>  
Methylprednisolone sodium succinate— $C_{26}H_{33}NaO_8$ .<sup>{R-29}</sup>  
Prednisolone— $C_{21}H_{28}O_5$ .<sup>{R-29}</sup>  
Prednisolone acetate— $C_{23}H_{30}O_6$ .<sup>{R-29}</sup>  
Prednisolone sodium succinate— $C_{25}H_{31}NaO_8$ .<sup>{R-29}</sup>  
Prednisone— $C_{21}H_{26}O_5 \cdot H_2O$ .<sup>{R-29}</sup>  
Triamcinolone— $C_{21}H_{27}FO_6$ .<sup>{R-29}</sup>  
Triamcinolone acetonide— $C_{24}H_{31}FO_6$ .<sup>{R-29}</sup>

**Molecular weight:**

Dexamethasone—392.46.<sup>{R-29}</sup>  
Dexamethasone sodium phosphate—516.40.<sup>{R-29}</sup>  
Hydrocortisone—362.46.<sup>{R-29}</sup>  
Isoflupredone acetate—420.47.<sup>{R-29}</sup>  
Methylprednisolone—374.47.<sup>{R-29}</sup>  
Methylprednisolone acetate—416.51.<sup>{R-29}</sup>  
Methylprednisolone sodium succinate—496.53.<sup>{R-29}</sup>  
Prednisolone—360.44.<sup>{R-29}</sup>  
Prednisolone acetate—402.48.<sup>{R-29}</sup>  
Prednisolone sodium succinate—482.50.<sup>{R-29}</sup>  
Prednisone—376.44.<sup>{R-29}</sup>  
Triamcinolone—394.43.<sup>{R-29}</sup>  
Triamcinolone acetonide—434.50.<sup>{R-29}</sup>

**Description:**

Dexamethasone USP—White to practically white, odorless, crystalline powder. Is stable in air. Melts at about 250° C, with some decomposition.<sup>{R-183}</sup>  
Dexamethasone Sodium Phosphate USP—White or slightly yellow, crystalline powder. Is odorless or has a slight odor of alcohol, and is exceedingly hygroscopic.<sup>{R-183}</sup>  
Flumethasone—A white or creamy white, odorless, crystalline powder.<sup>{R-18}</sup>  
Hydrocortisone USP—White to practically white, odorless, crystalline powder. Melts at about 215° C, with decomposition.<sup>{R-183}</sup>  
Methylprednisolone USP—White to practically white, odorless, crystalline powder. Melts at about 240° C, with some decomposition.<sup>{R-183}</sup>  
Methylprednisolone Acetate USP—White or practically white, odorless, crystalline powder. Melts at about 225° C, with some decomposition.<sup>{R-183}</sup>  
Methylprednisolone Sodium Succinate USP—White or nearly white, odorless, hygroscopic, amorphous solid.<sup>{R-183}</sup>  
Prednisolone USP—White to practically white, odorless, crystalline powder. Melts at about 235° C, with some decomposition.<sup>{R-183}</sup>  
Prednisolone Acetate USP—White to practically white, odorless, crystalline powder. Melts at about 235° C, with some decomposition.<sup>{R-183}</sup>  
Prednisolone Sodium Succinate for Injection USP—Creamy white powder with friable lumps, having a slight odor.<sup>{R-183}</sup>  
Prednisone USP—White to practically white, odorless, crystalline powder. Melts at about 230° C, with some decomposition.<sup>{R-183}</sup>  
Triamcinolone USP—White or practically white, odorless, crystalline powder.<sup>{R-183}</sup>  
Triamcinolone Acetonide USP—White to cream-colored, crystalline powder, having not more than a slight odor.<sup>{R-183}</sup>

**Solubility:**

Dexamethasone USP—Practically insoluble in water; sparingly soluble in acetone, in alcohol, in dioxane, and in methanol; slightly soluble in chloroform; very slightly soluble in ether.<sup>{R-183}</sup>  
Dexamethasone Sodium Phosphate USP—Freely soluble in water; slightly soluble in alcohol; very slightly soluble in dioxane; insoluble in chloroform and in ether.<sup>{R-183}</sup>  
Hydrocortisone USP—Very slightly soluble in water and in ether; sparingly soluble in acetone and in alcohol; slightly soluble in chloroform.<sup>{R-183}</sup>  
Methylprednisolone USP—Practically insoluble in water; sparingly soluble in alcohol, in dioxane, and in methanol; slightly soluble in acetone and in chloroform; very slightly soluble in ether.<sup>{R-183}</sup>

Methylprednisolone Acetate USP—Practically insoluble in water; soluble in dioxane; sparingly soluble in acetone, in alcohol, in chloroform, and in methanol; slightly soluble in ether.<sup>{R-183}</sup>

Methylprednisolone Sodium Succinate USP—Very soluble in water and in alcohol; very slightly soluble in acetone; insoluble in chloroform.<sup>{R-183}</sup>

Prednisolone USP—Very slightly soluble in water; soluble in methanol and in dioxane; sparingly soluble in acetone and in alcohol; slightly soluble in chloroform.<sup>{R-183}</sup>

Prednisolone Acetate USP—Practically insoluble in water; slightly soluble in acetone, in alcohol, and in chloroform.<sup>{R-183}</sup>

Prednisone USP—Very slightly soluble in water; slightly soluble in alcohol, in chloroform, in dioxane, and in methanol.<sup>{R-183}</sup>

Triamcinolone USP—Very slightly soluble in water, in chloroform, and in ether; slightly soluble in alcohol and in methanol.<sup>{R-183}</sup>

Triamcinolone Acetonide USP—Practically insoluble in water; sparingly soluble in dehydrated alcohol, in chloroform, and in methanol.<sup>{R-183}</sup>

## 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.<sup>{R-30}</sup> The glucocorticoids affect protein, carbohydrate, and lipid balance, while the mineralocorticoids affect water and electrolyte balance.<sup>{R-35}</sup> 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.<sup>{R-31}</sup> The effects are 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.<sup>{R-31}</sup> Some nonspecific effects may also occur with cell membrane contact alone at high hormone concentrations.<sup>{R-31}</sup> 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.<sup>{R-30; 33}</sup>

**Inflammation—**The exact mechanism of action for the glucocorticoids in decreasing inflammation is not known<sup>{R-14}</sup> but they decrease or prevent tissue responses to inflammatory processes,<sup>{R-30}</sup> 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.<sup>{R-31}</sup> 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.<sup>{R-31}</sup> They alter the distribution and function of peripheral leukocytes, decreasing their numbers at the site of inflammation.<sup>{R-14; 31}</sup> To accomplish this, they decrease the vascular adherence of neutrophils and decrease diapedesis, thus preventing neutrophils from reaching the site of inflammation,<sup>{R-36; 37}</sup> and they also decrease macrophage response to

migration inhibiting factor.<sup>{R-30}</sup> In addition, glucocorticoids also decrease production of cytokines and other mediators.<sup>{R-228}</sup>

**Immunosuppression**—In general, glucocorticoids are considered less immunosuppressive than anti-inflammatory;<sup>{R-38}</sup> 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 beneficial effect in immune-mediated disease.<sup>{R-38}</sup> The functional capacity of monocytes, macrophages, and eosinophils is decreased via inhibition of the formation of interleukins, and virus-induced interferon synthesis is inhibited.<sup>{R-31}</sup> The alteration of the movement and circulation of leukocytes may alter the immune response.<sup>{R-14; 31}</sup> 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.<sup>{R-31; 36; 193}</sup> Antibody production generally is inhibited only with high doses or with long-term administration.<sup>{R-31}</sup>

**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,<sup>{R-30; 31}</sup> 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.<sup>{R-35}</sup>

**Spinal cord trauma, acute**—Glucocorticoids may limit neural damage by preserving microcirculation by vasodilation, scavenging for free radicals, acting to control edema and inflammation, and blocking lipid peroxidation.<sup>{R-43}</sup>

**Induction of abortion and**

**Induction of parturition—**

**Cattle:** The corticosteroids are believed to suppress progesterone production by the placenta and adrenal gland and, when administered in the final days of pregnancy, mimic rising fetal cortisol to stimulate the initiation of natural parturition. After approximately 150 days of gestation in cattle, it is postulated that the placenta produces enough progesterone to maintain pregnancy even in the absence of a corpus luteum up until about 250 days of gestation. The luteolysis produced by administration of prostaglandin is not sufficient to induce abortion during this period, but the combination of dexamethasone and prostaglandin is very effective.<sup>{R-190; 191}</sup> Although corticosteroids may induce abortion any time after about 180 days of gestation, the combination of corticosteroid and prostaglandin is typically given to make abortion or early parturition more predictable.<sup>{R-110-114}</sup>

**Dogs:** The production of cortisol by the fetus also is believed to be part of the induction of parturition in dogs; therefore, the administration of exogenous glucocorticoids can be successful in inducing abortion in dogs after 28 days of gestation.<sup>{R-118}</sup>

#### **Other actions/effects:**

**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 and/or exogenous glucocorticoids inhibit the production of adrenocorticotropic hormone (ACTH) by the anterior pituitary gland, preventing the subsequent stimulation of cortisol production by ACTH.<sup>{R-31}</sup> 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 luteinizing hormone, and growth hormone.<sup>{R-31; 33}</sup> 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.<sup>{R-27}</sup> 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.<sup>{R-27}</sup>

**Bone effects**—Glucocorticoids inhibit osteoblasts and stimulate osteoclasts, thereby inhibiting bone healing.<sup>{R-31}</sup>

**Cardiovascular effects**—Glucocorticoids have direct positive chronotropic and inotropic actions on the heart.<sup>{R-31}</sup> They enhance vasoconstriction and decrease capillary permeability, including that induced by inflammation.<sup>{R-31}</sup> 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.<sup>{R-31}</sup>

**Central nervous system (CNS) effects**—Glucocorticoids are essential for normal adrenergic receptor sensitivity in the autonomic nervous system.<sup>{R-30}</sup> 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.<sup>{R-30; 33}</sup>

**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.<sup>{R-30}</sup>

**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.<sup>{R-31}</sup> Abnormal redistribution of fat can occur with long-term use. Glucocorticoids cause a decrease in synthesis of proteins and an increase in degradation.<sup>{R-30; 31}</sup> With prolonged use, muscle atrophy, thin skin, and delayed healing can result.<sup>{R-30}</sup>

#### **Absorption:**

**Oral**—In the dog, prednisolone and prednisone are absorbed rapidly and reach significant serum concentrations in less than 30 minutes.<sup>{R-100}</sup>

**Parenteral**—Esterification of a glucocorticoid affects its water and lipid solubility and the rate at which it is absorbed from the injection site.<sup>{R-30; 31}</sup> Succinate and phosphate esters are the most water-soluble esters and are rapidly absorbed from intramuscular, intravenous, or subcutaneous administration.<sup>{R-30}</sup> Acetate and acetone esters are poorly water-soluble and result in slow and sustained absorption from intramuscular depot injections.<sup>{R-30; 31}</sup>

**Note:** In the cow, 95% of an intramammary dose of 40 mg of prednisolone is absorbed systemically within 3 hours;<sup>{R-73}</sup> less than 5% is recovered in the milk.<sup>{R-73}</sup>

**Bioavailability**—Dexamethasone:

**Intramuscular administration**—

*Cattle:* 67%, with a dose of 0.1 mg per kg of body weight (mg/kg).<sup>{R-70}</sup>

*Horses:* 67 to 72%, with a dose of 0.1 mg/kg.<sup>{R-70}</sup>

**Oral**—*Horses:* 61 ± 19%, with a total dose of 10 mg.<sup>{R-68}</sup>

**Distribution:** Volume of distribution—

**Dexamethasone:**

*Cattle*—Area: 1.1 to 1.2 liters per kg (L/kg).<sup>{R-70}</sup>

*Dogs*—Area:

1.85 ± 1.16 L/kg, with a 0.01 mg/kg dose.<sup>{R-60}</sup>

6.41 ± 2.75 L/kg, with a 0.1 mg/kg dose.<sup>{R-60}</sup>

1.11 to 1.29 L/kg, with a 1 mg/kg dose.<sup>{R-61}</sup>

*Horses*—

Area: 0.906 to 0.966 L/kg.<sup>{R-67}</sup>

Steady state: 1.73 ± 0.48 L/kg.<sup>{R-68}</sup>

**Methylprednisolone:** *Dogs*—

Area: 1.76 ± 0.55 L/kg.<sup>{R-66}</sup>

Steady state:  $1.69 \pm 0.53$  L/kg.<sup>{R-66}</sup>

**Prednisolone:**

*Cattle*—Administered as the 21-sodium succinate ester: Area— $2.19 \pm 0.865$  L/kg.<sup>{R-74}</sup>

*Dogs*—Administered as the sodium succinate ester:

Area— $0.918 \pm 0.107$  L/kg.<sup>{R-65}</sup>

Steady state— $0.494$  L/kg.<sup>{R-102}</sup>

*Horses*—Administered as the 21-sodium succinate ester: Area— $0.561 \pm 0.132$  L/kg.<sup>{R-67}</sup>

*Pigs*—Apparent:  $1.2$  at  $0.2$  L/kg.<sup>{R-82}</sup>

*Rabbits*—Administered as the 21-sodium succinate ester: Steady state—

$1.44$  L/kg, with a  $0.15$  mg/kg dose.<sup>{R-78}</sup>

$2.14$  L/kg, with a  $3$  mg/kg dose.<sup>{R-78}</sup>

**Protein binding:**

Dexamethasone—*Rats*: High (83%).<sup>{R-81}</sup>

Methylprednisolone—*Rabbits*: High (77%).<sup>{R-80}</sup>

Prednisolone—*Dogs*: Moderate to high (51 to 84%, dose-dependent).<sup>{R-102}</sup>

**Biotransformation:** Hepatic metabolism is the main elimination pathway of corticosteroids in animals.<sup>{R-79}</sup> In addition, many glucocorticoids are administered in a form that must undergo hydrolysis or hepatic biotransformation to become active. Prednisone and cortisone are prodrugs that must be converted by the liver to prednisolone and hydrocortisone, respectively, to have glucocorticoid activity.<sup>{R-34}</sup> 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.<sup>{R-100}</sup> Hepatic metabolism of prednisone to active 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 compared to prednisolone<sup>{R-100}</sup> should not be significantly different in dogs without severe hepatic compromise.

**Methylprednisolone/methylprednisone**—In rabbits, methylprednisolone is rapidly and reversibly converted to methylprednisone.<sup>{R-80}</sup> Plasma concentration of methylprednisolone is generally greater than methylprednisone regardless of whether methylprednisolone or methylprednisone is administered,<sup>{R-80}</sup> however, methylprednisolone is only  $67 \pm 15\%$  available from methylprednisone in the rabbit.<sup>{R-80}</sup>

*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.<sup>{R-66; 120}</sup> However, in the dog only 46% of an intramuscular dose of 4 mg/kg becomes available as methylprednisolone base.<sup>{R-66}</sup>

**Methylprednisolone sodium succinate:** Only 43% of an intravenous dose becomes available as methylprednisolone base<sup>{R-66}</sup> in the dog.

**Prednisolone acetate:** Completely available as the prednisolone base after intramuscular administration.<sup>{R-67}</sup>

**Prednisolone 21-sodium succinate:** Appears to be immediately hydrolyzed to prednisolone in the horse after intravenous administration.<sup>{R-67}</sup> Completely available as the prednisolone base after intramuscular administration.<sup>{R-74}</sup>

**Half-life:**

**Absorption**—Intramuscular administration:

Dexamethasone—*Cattle*: 1.2 to 1.6 hours, with a dose of 0.1 mg/kg.<sup>{R-70}</sup>

Methylprednisolone acetate—*Dogs*: 69 hours, with a dose of 4 mg/kg.<sup>{R-66}</sup>

**Distribution**—Intravenous administration:



Dexamethasone—

*Cattle*: 0.13 to 0.18 hour.<sup>{R-70}</sup>

*Dogs*: 0.13 to 0.5 hour.<sup>{R-60; 61}</sup>

Prednisone—

*Dogs*: 0.25 hour.<sup>{R-105}</sup>

*Monkeys*: 0.55 hour.<sup>{R-105}</sup>

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.<sup>{R-70}</sup>

*Dogs*:

3.2 hours, with a 0.01 mg/kg dose.<sup>{R-60}</sup>

6.9 hours, with a 0.1 mg/kg dose.<sup>{R-60}</sup>

2 to 2.3 hours, with a 1 mg/kg dose.<sup>{R-61; 70}</sup>

*Horses*: 0.88 hour;<sup>{R-67}</sup> 2.63 ± 1.19 hours.<sup>{R-68}</sup>

Hydrocortisone—*Dogs*: 0.91 ± 0.06 minutes.<sup>{R-103}</sup>

Methylprednisolone—

*Cattle*: 1.43 ± 0.32 hours.<sup>{R-120}</sup>

*Dogs*: 1.35 ± 0.13 hours;<sup>{R-16}</sup> 1.67 to 2.64 hours.<sup>{R-66}</sup>

*Horses*: 2.87 ± 1.5 hours.<sup>{R-121}</sup>

*Rabbits*: 1.82 hours.<sup>{R-80}</sup>

Methylprednisolone—*Rabbits*: 2.1 hours.<sup>{R-80}</sup>

Prednisolone—

*Cattle*: 3.61 ± 1.18 hours, administered as the sodium succinate ester.<sup>{R-74}</sup>

*Dogs*:

1.3 hours, with a dose of 0.39 mg/kg.<sup>{R-16; 102}</sup>

0.25 to 0.88 hour, with a dose of 1.7 to 3.4 mg/kg, administered as the sodium phosphate ester.<sup>{R-104}</sup>

2.77 ± 0.53 hours, with a dose of 8.8 mg/kg, administered as the sodium succinate ester.<sup>{R-65}</sup>

*Horses*: 1.65 hours, administered as the 21-sodium succinate ester.<sup>{R-67}</sup>

*Pigs*: 0.73 ± 0.15 hour.<sup>{R-82}</sup>

Prednisone—

*Dogs*: 1.4 hours.<sup>{R-105}</sup>

*Monkeys*: 1.3 hours.<sup>{R-105}</sup>

Triamcinolone—*Dogs*: 1.95 ± 0.12 hours.<sup>{R-103}</sup>

Intra-articular administration: Elimination of methylprednisolone after methylprednisolone acetate administration:

*Cattle*—With a total dose of 200 mg.<sup>{R-120}</sup>

First phase—0.92 ± 0.44 hour.

Second phase—18.7 ± 6.7 hours.

Third phase—18.1 ± 3.4 days.

*Horses*—With a total dose of 110 mg.<sup>{R-121}</sup>

First phase—10 hours.

Second phase—4.79 days (range of 1.54 to 8.6 days).

**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<sup>{R-11}</sup> and sodium succinate<sup>{R-7}</sup> esters. However, these products will only act as rapidly as their base glucocorticoids; methylprednisolone or prednisone 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.

Oral—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.<sup>{R-100}</sup>

#### Concentrations:

Endogenous serum cortisol, baseline—

*Cats*: Ranges from 3 to 82.8 nanograms per mL (nanograms/mL) (mean  $17 \pm 2.8$ ).<sup>{R-140; 155}</sup>

*Cattle*: 3 to 15 nanograms/mL.<sup>{R-70; 74; 75; 120}</sup>

*Dogs*:  $15.8 \pm 8$  nanograms/mL.<sup>{R-102}</sup>

*Horses*: 43 to 87 nanograms/mL.<sup>{R-67; 121; 151; 178}</sup>

*Sheep*: 6.2 to 6.9 nanograms/mL.<sup>{R-76}</sup>

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.<sup>{R-151}</sup> In cats and dogs, there is no evidence that cortisol concentrations vary in a circadian pattern.<sup>{R-155; 156; 208; 209}</sup>

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.<sup>{R-70}</sup>

Intravenous—*Horses*: 20 to 35 nanograms/mL at 15 minutes after a total dose of 5 mg per animal.<sup>{R-69}</sup>

Oral—*Horses*:  $4.9 \pm 0.17$  nanograms/mL at  $1.3 \pm 0.5$  hours, with a total dose of 10 mg per animal.<sup>{R-68}</sup>

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.<sup>{R-74}</sup>

*Horses*:  $59 \pm 13.5$  nanograms/mL at 10 hours<sup>{R-67}</sup> 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).<sup>{R-100}</sup>

Prednisone: Oral—*Dogs*: 205 nanograms of prednisolone per mL at 1.3 hours after a total dose of one 5-mg tablet per animal ( $0.53$  to  $0.29$  mg/kg).<sup>{R-100}</sup>

Note: Peak serum prednisolone concentrations were always approximately twice as high as peak serum prednisone concentrations, regardless of whether oral prednisone or prednisone was administered;<sup>{R-100}</sup> however, the combined prednisone and prednisolone areas under the serum concentration-versus-time curves were similar for oral prednisone and prednisolone administration.<sup>{R-100}</sup>

Peak concentrations, other—Intra-articular administration:

Methylprednisolone acetate—

*Cattle*:

Serum methylprednisolone— $7.8 \pm 5.7$  nanograms/mL at  $4.5 \pm 1.3$  hours, with a total dose of 200 mg per animal (single joint treated).<sup>{R-120}</sup>

Synovial methylprednisolone—4 mg/mL at 20 minutes, with a total dose of 200 mg per animal (single joint treated).<sup>{R-120}</sup>

*Horses*:

Serum methylprednisolone—Less than 5 nanograms/mL for the first 24 hours after intra-articular administration, with a total dose of 110 mg.<sup>{R-121}</sup>

Synovial methylprednisolone— $138 \pm 83$  mcg/mL at 2 hours and  $174 \pm 175$  mcg/mL at 10 hours, with a total dose of 110 mg.<sup>{R-121}</sup>

Note: Although variable and not well defined, synovial methylprednisolone concentrations are detectable for up to 39 days (range 4 to 39 days).<sup>{R-121}</sup>

Triamcinolone—*Horses*:

Serum triamcinolone—4.3 nanograms/mL at 4 hours, with a single dose of 6 mg.<sup>{R-129}</sup>

Synovial triamcinolone—7.5 mcg/mL 1 day after injection, with a single dose of 6 mg.<sup>{R-129}</sup>

Note: Synovial triamcinolone concentrations are detectable for up to 14 days.<sup>{R-129}</sup>

**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<sup>(R-61)</sup> 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.<sup>(R-134)</sup> In other situations, adrenocortical suppression may continue even though there are no longer measurable serum levels<sup>(R-74)</sup> or clinical effects.<sup>(R-139)</sup> 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).<sup>(R-34)</sup> Intermediate-acting bases (12 to 36 hours) include methylprednisolone, prednisolone, prednisone, and triamcinolone.<sup>(R-34)</sup> Long-acting bases (36 to 72 hours) include dexamethasone and flumethasone.<sup>(R-31;34)</sup> 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).<sup>(R-140)</sup>

Oral—32 hours below detectable concentrations after a dose of 0.1 mg/kg.<sup>(R-155)</sup>

*Dogs:* 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.<sup>(R-61)</sup>

*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.<sup>(R-67;145)</sup>

Intravenous—48 hours below baseline concentration after a dose of 0.2 mg/kg.<sup>(R-151)</sup> Suppression began 2 hours after administration.<sup>(R-151)</sup>

Oral—72 hours below baseline concentrations after a dose of 0.2 mg/kg.<sup>(R-151)</sup> Suppression began 2 hours after administration.<sup>(R-151)</sup>

*Pigeons:* Intravenous—

Less than 24 hours below baseline concentration with a dose of 0.5 micrograms per kg of body weight (mcg/kg).<sup>(R-146)</sup>

52 hours below baseline concentration with a dose of 500 mcg/kg.<sup>(R-146)</sup>

Methylprednisolone—*Cats:* Oral—Adrenocorticotrophic 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.<sup>(R-139)</sup>

Methylprednisolone acetate—

*Cattle:* Intra-articular—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.<sup>(R-120)</sup>

*Dogs:* Intramuscular—3 to 4 weeks below baseline concentration after administration of 2.5 mg/kg.<sup>(R-135)</sup> Adrenal response to adrenocorticotrophic hormone (ACTH) was suppressed for at least 5 weeks.<sup>(R-135)</sup>

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.<sup>(R-138)</sup>

*Horses:* Intra-articular—6 to 18 hours below baseline concentration after an intra-articular injection of 120 mg as a total dose.<sup>(R-151)</sup>

Prednisolone—

*Cattle:* Intramuscular or intravenous—2 days below baseline concentration after a prednisolone sodium succinate dose of 0.6 mg/kg.<sup>(R-74)</sup>

*Horses:* Intramuscular or intravenous—24 hours below baseline

- concentration after a dose of 0.6 mg/kg.<sup>{R-67}</sup>
- Pigeons*: Intravenous—  
 Less than 24 hours below baseline concentration after a dose of 0.7 mcg/kg.<sup>{R-146}</sup>  
 48 hours below baseline concentration after a single dose of 3500 mcg/kg (3.5 mg/kg).<sup>{R-146}</sup>
- 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; prednisolone was no longer detectable in the blood after 6 days.<sup>{R-74}</sup>  
*Horses*: Intramuscular—21 days below baseline concentration and 5 days at nondetectable or low concentrations after a dose of 0.6 mg/kg.<sup>{R-67}</sup>
- Prednisone—*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.<sup>{R-136}</sup> ACTH response was suppressed beginning 1 week after treatment and remained suppressed for most of the treatment period.<sup>{R-136}</sup>  
 Dose of 0.55 mg/kg every 24 hours: Below the limits of the assay (1 mcg of cortisol per decaliter of serum) after 1 week of therapy until at least the end of therapy.<sup>{R-136}</sup> Suppression of ACTH response was noted when first measured after 1 week of therapy and lasted at least until the cessation of treatment.<sup>{R-136}</sup>  
 Dose of 0.55 mg/kg every 12 hours: Significantly reduced below baseline after 14 days of therapy until a return to baseline 2 weeks after the end of treatment.<sup>{R-137}</sup>  
 Dose of 1.1 mg/kg every 48 hours: Serum cortisol was not significantly affected during the treatment period; however, suppression of ACTH response was noted after 2 to 3 weeks of therapy.<sup>{R-136}</sup>
- Triamcinolone—*Horses*:  
 Intra-articular—5 days below baseline concentration after a total dose of 6 mg per animal (single joint treated).<sup>{R-129}</sup>  
 Intramuscular—8 days below detectable concentrations and 14 days until a return to baseline concentration after a dose of 0.044 mg/kg.<sup>{R-148}</sup>

**Elimination:** Hepatic metabolism is the main elimination pathway of corticosteroids in animals;<sup>{R-79}</sup> however, biliary excretion, renal metabolism, and renal clearance contribute to a small degree in some species.<sup>{R-79}</sup>

Dexamethasone—Total clearance:

*Cattle*—2.4 to 2.6 mL per minute per kg (mL/min/kg).<sup>{R-70}</sup>

*Dogs*—

5.41 ± 1.74 mL/min/kg, with a 0.01 mg/kg dose.<sup>{R-60}</sup>

9.67 ± 2.7 mL/min/kg, with a 0.1 mg/kg dose.<sup>{R-60}</sup>

6.4 to 6.57 mL/min/kg, with a 1 mg/kg dose.<sup>{R-61}</sup>

*Horses*—

7.98 at 1.06 mL/min/kg, with a total dose of 10 mg per animal.<sup>{R-68}</sup>

12.4 to 12.9 mL/min/kg, with a dose of 0.05 mg/kg.<sup>{R-67}</sup>

Methylprednisolone—In the dog, 25 to 34% of an oral or intramuscular dose of methylprednisolone acetate is eliminated in the urine and 27 to 52% in the feces.<sup>{R-101}</sup> Multiple metabolites are found in the urine and feces.<sup>{R-101}</sup>

Total clearance:

*Dogs*—9 ± 1.2 mL/min/kg.<sup>{R-66}</sup>

*Horses*—14.7 mL/min/kg.<sup>{R-121}</sup>

*Rabbits*—8 mL/min/kg.<sup>{R-80}</sup>

Methylprednisone—Total clearance: *Rabbits*—30.4 mL/min/kg.<sup>{R-80}</sup>

Prednisolone—In the cow, 42 to 46% of an intravenous injection of 0.067 mg of prednisolone per kg of body weight is eventually eliminated in the urine.<sup>{R-73}</sup> Less than 0.2% is distributed into the milk and it has been assumed that the majority is eliminated in the feces.<sup>{R-73}</sup>

Total clearance:

*Cattle*— $7.5 \pm 0.83$  mL/min/kg (prednisolone administered as the 21-sodium succinate ester).<sup>{R-74}</sup>

*Dogs*— $8.4$  mL/min/kg;  $3.96 \pm 0.96$  mL/min/kg (administered as the sodium succinate ester).<sup>{R-65; 102}</sup>

*Horses*— $3.92 \pm 0.66$  mL/min/kg (administered as the 21-sodium succinate ester).<sup>{R-67}</sup>

*Pigs*— $25.7 \pm 2.1$  mL/min/kg.<sup>{R-82}</sup>

*Prednisone—Dogs*: After an intravenous or oral dose of 1 mg/kg, 61 to 72% of the dose is excreted in the urine, but only 2% as unmetabolized prednisone and 6% as prednisolone.<sup>{R-104; 105}</sup>

*Triamcinolone—Dogs*: Elimination is equally divided between feces and urine after an intravenous dose of 2 mg/kg.<sup>{R-103}</sup> 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.<sup>{R-103}</sup>

## 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.<sup>{R-36}</sup>

### Pregnancy/Reproduction

*All species*: Corticosteroid administered systemically during the last trimester of pregnancy may induce the first stage of parturition.<sup>{R-5; 6; 15; 18; 19}</sup> If induced prematurely, labor may be followed by dystocia, fetal death, retained placenta, and/or metritis.<sup>{R-5; 6; 15; 18; 19}</sup> The likelihood of inducing abortion in ruminants is highest with the C16-methylated products, such as dexamethasone or flumethasone.<sup>{R-213}</sup> Risk of abortion is still present but to a lesser degree with administration of isoflupredone or prednisolone.<sup>{R-213}</sup>

*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).<sup>{R-5; 6; 15; 19}</sup>

*Rabbits and rodents*: Corticosteroids administered during pregnancy have caused cleft palate.<sup>{R-5; 6; 15; 19}</sup>

### Lactation

#### *Cattle*:

*Dexamethasone*—Dexamethasone concentrations in milk have been measured to be 0.3 to 0.5 times the plasma concentration in healthy cows.<sup>{R-71; 72}</sup> 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).<sup>{R-72}</sup>

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.<sup>{R-105}</sup> Three days after administration, milk dexamethasone concentrations had dropped to 1 nanogram per mL.<sup>{R-205}</sup>

*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.<sup>{R-205}</sup>

*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.<sup>{R-73}</sup>

### 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 (» = 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;<sup>(R-81)</sup> 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<sup>(R-119)</sup> and possibly other corticosteroids can prevent or delay the generally predictable estrus in response to norgestomet and estradiol valerate in cattle)

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;<sup>(R-81)</sup> 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;<sup>(R-194)</sup> short-term anti-inflammatory dosing of corticosteroids is not considered to interfere significantly with antibody response to vaccination,<sup>(R-203; 204)</sup> although there is not a preponderance of research in this area)

**Human drug interactions and/or related problems<sup>(R-2)</sup>**

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 I*; 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 hypernatremia 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)  
(concurrent use of potassium-depleting diuretics with corticosteroids may result in severe hypokalemia; monitoring of serum potassium concentration and cardiac function is recommended)  
(effects of potassium-sparing diuretics and/or corticosteroids on serum potassium concentration may be decreased during concurrent use; monitoring of serum potassium concentration is recommended)

Ephedrine or  
Phenobarbital or  
Phenytoin or  
Rifampin

(concurrent use may increase the metabolic clearance of corticosteroids; corticosteroid dosage adjustment may be required during and following concurrent use)

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)

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)

Mexiletine

(concurrent use with glucocorticoids may accelerate mexiletine metabolism, leading to decreased mexiletine 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 in the treatment of arthritis may provide additive therapeutic benefit and permit glucocorticoid dosage reduction, glucocorticoids may increase salicylate excretion and reduce salicylate plasma concentrations)



so that the salicylate dosage requirement may be increased; salicylism may occur when glucocorticoid dosage is subsequently decreased or discontinued, especially in patients receiving large [antirheumatic] doses of salicylates; also, the risk of gastrointestinal ulceration or hemorrhage may be increased during concurrent use)

**Sodium-containing medications or foods**

(concurrent use with pharmacologic doses of glucocorticoids may result in edema and increased blood pressure, possibly to hypertensive levels)

(although patients receiving replacement doses of glucocorticoids may require sodium supplementation, adjustment of dietary sodium intake may be required when a medication having a high sodium content is also administered concurrently)

**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 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)

**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 (» = major clinical significance):

**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<sup>(R-134)</sup>)

**With physiology/laboratory test values**

**Adrenal function as assessed by ACTH stimulation or measurement of plasma or urinary free cortisol**

(may be decreased with chronic glucocorticoid treatment<sup>(R-31)</sup>)

**Alanine aminotransferase (ALT [SGPT])<sup>(R-5; 19; 148)</sup> and**

**Alkaline phosphatase (ALP)<sup>(R-5; 19; 147; 148)</sup> and**

**Gamma-glutamyltransferase (GGT)<sup>(R-147; 148)</sup>**

(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<sup>(R-161)</sup>)

Eosinophil count  
(in dogs and other species, eosinopenia may occur<sup>(R-152; 153; 161)</sup>)

Globulins, alpha-2/haptoglobin  
(although the significance is not known, alpha-2-globulin measured in the serum will increase in dogs<sup>(R-152)</sup> and sheep; the increase may be primarily the haptoglobin component<sup>(R-154)</sup>)

Glucose  
(hyperglycemia may occur)

Lymphocyte count  
(in dogs and rodents, count may be decreased;<sup>(R-36; 153; 161)</sup> in cattle and cats, it is less likely to be altered<sup>(R-36)</sup>)

Monocyte count  
(in dogs, count may be increased;<sup>(R-156; 161)</sup> in other species, it is less likely to be altered<sup>(R-36)</sup>)

Neutrophil count  
(in cattle, dogs, goats, lambs, and other species, count may be increased<sup>(R-36; 156; 161)</sup>)

Testosterone, serum  
(in bulls and rams, dexamethasone can decrease serum testosterone levels<sup>(R-169; 170)</sup>)

Triiodothyronine (T<sub>3</sub>) and  
Thyroxine (T<sub>4</sub>), total and free and  
Thyrotropin stimulation test (TSH) and  
Thyrotropin-releasing hormone test (TRH)  
(in dogs, with anti-inflammatory dosing [oral prednisone, 0.55 mg/kg every 12 hours], baseline serum T<sub>3</sub> is reduced while T<sub>4</sub> is unaffected and the thyroid becomes hyper-responsive to TSH after 2 to 4 weeks;<sup>(R-130)</sup> with immunosuppressive dosing [oral prednisolone, 1.1 mg/kg every 12 hours], T<sub>3</sub>, T<sub>4</sub>, and fT<sub>4</sub> are decreased as early as 24 hours after initiation of treatment, but response to TSH and TRH tests is increased, allowing the latter two tests to be used to differentiate primary hypothyroidism from changes due to prednisolone administration;<sup>(R-131)</sup> in horses, 5 days of treatment with dexamethasone [intramuscular, 0.04 mg/kg every 24 hours] can significantly blunt TSH response so that normal horses do not show the twice baseline T<sub>4</sub> concentration response considered normal<sup>(R-133)</sup>)

#### **Human laboratory value alterations<sup>(R-2)</sup>**

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 *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:

With results of dexamethasone suppression tests

##### *Due to other medications*

- Benzodiazepines (high doses) or
- Cyproheptadine (high doses) or
- Glucocorticoid therapy, long-term or
- Indomethacin  
(may cause false-negative results in test for endogenous depression)
- Ephedrine or
- Estrogens (high doses) or
- Hepatic enzyme-inducing agents  
(may cause false-positive results in tests for Cushing's disease or endogenous depression)

##### *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
  - (may cause false-positive results in test for endogenous depression)
- Adrenal insufficiency or
- Hypopituitarism
  - (may cause false-negative results in test for endogenous depression)
- 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 through a complicated feedback mechanism)
  - Nitroblue-tetrazolium test
    - (false-negative test results may occur)
  - 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 hypopituitarism is generally not recommended)
  - Skeletal imaging using technetium Tc 99m medronate, technetium Tc 99m oxidronate, or technetium Tc 99m pyrophosphate
    - (long-term use of glucocorticoids may induce bone calcium depletion, thus causing decreased bone uptake of these diagnostic aids)
  - Skin tests, including tuberculin and histoplasmin skin tests and patch tests for allergy
    - (reactions may be suppressed, especially with daily administration of large doses of corticosteroids)
  - Thyroid <sup>123</sup>I or <sup>131</sup>I uptake
    - (may be decreased)
- With physiology/laboratory test values
  - Calcium, serum
    - (concentrations may be decreased)
  - Glucose, blood and urine
    - (concentrations may be increased because of intrinsic hyperglycemic activity)
  - Hypothalamic-pituitary-adrenal (HPA) axis function as assessed by:
    - Adrenocorticotrophic hormone (ACTH, corticotropin) or
    - Cortisol, blood or
    - Cortisol, urine or
    - 17-Hydroxycorticosteroids, urine (17-OHCS) or
    - 17-Ketosteroids, urine (17-KS)
      - (concentrations may be decreased with pharmacologic doses of glucocorticoids)
  - Lipid (fatty acid), serum
    - (concentrations may be increased)
  - Platelet count
    - (may be increased or decreased)
  - Polymorphonuclear leukocyte count
    - (may be increased)
  - Potassium, serum
    - (concentrations may be decreased because of increased potassium excretion, especially with agents having significant mineralocorticoid activity)
  - Sodium, blood
    - (concentrations may be increased because of sodium retention, especially with glucocorticoids having significant mineralocorticoid activity)
  - Uric acid, serum
    - (concentrations may be increased in patients with acute

leukemia; may be decreased in other patients because of weak uricosuric effect)  
White blood cell count  
(may be decreased)

### 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 (» = 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<sup>{R-15; 16}</sup>)

*For all routes of administration*

- Corneal ulcers<sup>{R-14}</sup>  
(in corneal ulceration that is not due to underlying disorders responsive to glucocorticoids, the ability to fight infection may be suppressed and healing delayed with administration of either ophthalmic or systemic corticosteroids; ophthalmic corticosteroids are generally considered contraindicated if corneal ulceration exists; systemic corticosteroids are thought by many to pose a much lower risk of exacerbating a corneal ulcer, although no corroborating evidence to confirm this could be found<sup>{R-223}</sup>)
- » Gastrointestinal ulcers<sup>{R-14; 15; 16}</sup>  
(may be exacerbated by glucocorticoid administration)
- Hyperadrenocorticism (Cushing's syndrome)<sup>{R-5; 6; 14; 15; 16}</sup>  
(with the exception of dexamethasone suppression tests, the administration of glucocorticoids to hyperadrenal animals is counterproductive)
- » Infections, bacterial, uncontrolled or
- » Infections, viral<sup>{R-14}</sup> or
- » Mycosis, systemic<sup>{R-164; 165}</sup> or
- » Tuberculosis<sup>{R-14; 15; 16; 22}</sup>  
(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)

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

*For all routes of administration*

- Abdominal surgery, extensive
- Bone fractures, severe or
- 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<sup>{R-213}</sup>)
- Congestive heart failure<sup>{R-5; 6; 14; 15; 16}</sup> or
- Hypertension<sup>{R-14; 15; 16}</sup>  
(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<sup>{R-31}</sup>)
- Diabetes mellitus<sup>{R-5; 6; 14; 15; 16}</sup>  
(glucocorticoids may increase insulin requirement<sup>{R-14}</sup>)
- Renal function impairment<sup>{R-5; 6; 14; 15; 16}</sup>  
(agents with mineralocorticoid effects may increase fluid retention and edema)
- Thrombophlebitis<sup>{R-14; 15; 16}</sup>  
(may increase risk of thrombophlebitis)

### Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = 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;**<sup>{R-20}</sup>  
**anorexia**—uncommon;<sup>{R-5; 14; 22}</sup> **bone resorption or inhibition of bone growth;**<sup>{R-30; 33}</sup> **collagen synthesis inhibition;**<sup>{R-30; 33}</sup> **decreased growth rate;**<sup>{R-171}</sup> **delayed bone and wound healing;**<sup>{R-19}</sup> **diarrhea;**<sup>{R-5; 14; 22}</sup> **suppression of endogenous steroid production;**<sup>{R-6}</sup> **fever, reduced;**<sup>{R-19}</sup> **gastrointestinal irritation/ulceration/perforation;**<sup>{R-166; 167}</sup> **hematopoietic changes; hypotension, acute**—may occur with rapid parenteral administration of formulations containing polyethylene glycol or propylene glycol as a vehicle;<sup>{R-127}</sup> **hypertension;**<sup>{R-31}</sup> **negative nitrogen balance;**<sup>{R-19}</sup> **panting;**<sup>{R-31}</sup> **potassium loss, sodium retention, and fluid retention**<sup>{R-214}</sup>—may occur with corticosteroids having some mineralocorticoid effects, such as hydrocortisone, isoflupredone, prednisolone, or prednisone; **recrudescence of latent infections**<sup>{R-159}</sup> **or decreased resistance to infectious agents;**<sup>{R-19; 159; 160; 164; 165}</sup> **suppressed inflammation;**<sup>{R-19}</sup> **weight gain or weight loss**<sup>{R-5; 6; 14; 18}</sup>

Note: Administration of corticosteroids always has the potential for causing a *suppression of endogenous production of steroids*.<sup>{R-6}</sup> The likelihood and degree of suppression increases with length of therapy.

*Gastrointestinal irritation/ulceration/perforation* are considered most likely with high doses or long-term administration of corticosteroids. Colonic perforation has been noted as a sequela to neurosurgery, in particular, surgery for intervertebral disk herniation, and the high doses of corticosteroids typically administered before and after surgery.<sup>{R-166}</sup> Gastrointestinal perforation and other serious gastrointestinal problems have been considered uncommon side effects of short-term corticosteroid therapy, but certain factors, such as surgery or the administration of high doses, may increase the incidence.<sup>{R-166}</sup>

*Hematopoietic changes* vary from species to species. Mature circulating neutrophilia occurs in many species, including cattle, dogs, goats, and lambs, but in the early response this is considered primarily a redistribution, rather than an increase in production.<sup>{R-36}</sup> Lymphopenia occurs in dogs and rodents; however, in dogs this occurs by redistribution and in mice, rabbits, and rats, it occurs from direct cytotoxicity.<sup>{R-36}</sup> In cats and cattle, lymphopenia is not a predictable finding.<sup>{R-36}</sup> Although decreased monocyte counts occur in human patients with corticosteroid administration, monocytosis occurs in dogs and monocyte count responses are not otherwise significant in other species.<sup>{R-36}</sup>

Increased protein degradation and conversion of proteins to carbohydrates lead to a *negative nitrogen balance* or catabolic state with administration of corticosteroids.<sup>{R-19}</sup>

*Reduced fever* and *suppressed inflammation* become side effects when they are undesirable, as in cases where signs of infection are suppressed and more serious infection is allowed to occur before diagnosis.

Glucocorticoids alter the immune system through a variety of effects on cells and cell mediators.<sup>{R-38}</sup> *Recrudescence of latent infections*<sup>{R-159}</sup> *or decreased resistance to infectious agents* can occur, although

the specific situations in which they will occur is not always easily predicted. One study investigated the effects of immunosuppressive or anti-inflammatory dosages of prednisolone administered with doxycycline to dogs experimentally infected with *Rickettsia rickettsii*.<sup>{R-207}</sup> They found no significant change in outcome in this disease model, other than an increased duration of rickettsemia with immunosuppressive, but not anti-inflammatory, dosing. There was a mild decrease in diagnostic antibody titers but comparison of acute and convalescent titers was not affected.<sup>{R-207}</sup> Immunosuppressive therapy can obviously affect defenses against pathogens, but even with the administration of lower doses the beneficial effects must be weighed against the cell inhibitory effects in the face of infection.

#### Cats

**Diarrhea;**<sup>{R-5; 19}</sup> **vomiting**<sup>{R-5; 19}</sup>

Note: Although cats are reported to be more resistant to the effects of corticosteroids than dogs<sup>{R-156}</sup> and there are few documented side/adverse effects, many of the effects listed for dogs and all species are considered potential feline problems with sufficient dose and duration of administration.

#### Cattle

**Decreased milk production, temporary;**<sup>{R-215; 216}</sup> **hypokalemia syndrome;**<sup>{R-214}</sup> **sperm defects;**<sup>{R-169}</sup> **termination of pregnancy**<sup>{R-110-114; 190; 191}</sup>

Note: *Hypokalemia* has been noted in cattle prone to anorexia or ketosis when treated with repeated doses of isoflupredone,<sup>{R-214}</sup> a corticosteroid with some mineralocorticoid effect. It is not yet known what dairy management factors may also contribute to this effect.

A significant rise in visible *sperm defects* occurs after intramuscular administration of 20 mg of dexamethasone a day as a total dose (approximately 0.04 mg/kg) for 7 days;<sup>{R-169}</sup> the effects appear to be reversed within 6 weeks of the end of treatment.

*Termination of pregnancy* will occur with administration of C16-methylated corticosteroids, including dexamethasone and flumethasone, beginning in mid-gestation to end of gestation.

#### Dogs

**Adrenocortical atrophy;**<sup>{R-136}</sup> **alopecia;**<sup>{R-38}</sup> **calcinosis cutis;**<sup>{R-38}</sup> **diabetes mellitus;**<sup>{R-158}</sup> **diarrhea;**<sup>{R-5; 14; 19; 22}</sup> **ecchymosis;**<sup>{R-14}</sup> **hematopoietic changes, including neutrophilia, lymphopenia, and eosinopenia;**<sup>{R-38}</sup> **hepatopathy** (hepatomegaly);<sup>{R-20; 148}</sup> **hyperadrenocorticism (Cushing's syndrome)** (decreased hair growth, hepatomegaly, lethargy, muscle weakness and atrophy,<sup>{R-30; 38}</sup> pendulous abdomen, polyuria/polydipsia, skin atrophy<sup>{R-30; 33; 38}</sup>)—generally with prolonged use and/or high dosage; **hyperglycemia**<sup>{R-38}</sup> **from gluconeogenesis and possibly insulin resistance;**<sup>{R-157}</sup> **hyperlipidemia, fasting;**<sup>{R-136}</sup> **increased appetite; inelasticity of skin;**<sup>{R-38}</sup> **osteoporosis, increased incidence of**—primarily in older dogs;<sup>{R-19}</sup> **polydipsia/polyuria;**<sup>{R-5; 14; 148}</sup> **termination of pregnancy;**<sup>{R-118}</sup> **thyroid hormone metabolism alterations;**<sup>{R-132}</sup> **urinary tract infection**—up to 40% of dogs on chronic corticosteroid therapy for 6 months to 5 years;<sup>{R-163}</sup> **vomiting**<sup>{R-5; 14; 19}</sup>

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 hyperlipidemia, focal hepatocellular fatty changes, and skin atrophy.*<sup>{R-136}</sup>

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.<sup>{R-158}</sup>

*Hepatopathy* or liver changes associated with glucocorticoid administration have been noted in some cases as early as the day after initiation of treatment,<sup>{R-148}</sup> but the degree and pattern of

the response varies.<sup>{R-152}</sup> Hepatocytes become swollen and vacuolated<sup>{R-148; 149; 152}</sup> and this initially may be due to hepatocellular accumulation of glycogen,<sup>{R-148; 149}</sup> of water, or of some combination of components. Laboratory value alterations associated with glucocorticoid administration include increased serum gamma-glutamyltransferase (SGGT; 23-fold increase in one study<sup>{R-148}</sup>), serum alkaline phosphatase (ALP; 64-fold in one study<sup>{R-148}</sup>), alanine aminotransferase (ALT [SGPT]; 10-fold in one study<sup>{R-148}</sup>) and normal to increased sulfobromophthalein sodium excretion test (BSP);<sup>{R-38; 147-150}</sup> however, alterations in enzymes are not always proportional to degree of histologic change in hepatic tissue.<sup>{R-152}</sup> Severe hepatocellular changes may be present before enzymes are significantly elevated.<sup>{R-152}</sup> Although the predominance of ALP compared to the elevation of other enzymes is considered a marker of cholestasis,<sup>{R-147; 148}</sup> 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.<sup>{R-148}</sup> Steroid hepatopathy is considered reversible in many dogs when corticosteroid therapy is ended; however, the return to normal may be prolonged in some animals.<sup>{R-150}</sup>

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

*Urinary tract infections* are as likely to occur in dogs receiving long-term alternate-day anti-inflammatory therapy as in those treated daily.<sup>{R-163}</sup>

Abnormal amylase and lipase values can occur in dogs in response to glucocorticoids without clinical *pancreatitis*.<sup>{R-161}</sup> A definite connection between long-term corticosteroid administration and induction of clinical pancreatitis has not been shown, although mild pancreatic inflammation has been demonstrated.<sup>{R-101}</sup> The risk of pancreatitis may be increased by concurrent administration of a glucocorticoid with azathioprine.<sup>{R-127}</sup>

#### Horses

**Hepatopathy**—rare;<sup>{R-150}</sup> **laminitis**—has been reported in association with dexamethasone, methylprednisolone, and triamcinolone administration;<sup>{R-5; 22; 77; 150}</sup> **lethargy**—with doses higher than labeled doses;<sup>{R-6}</sup> **long, shaggy haircoat (hirsutism)**<sup>{R-38}</sup>

With intra-articular injections

**Arthritis, septic**;<sup>{R-128}</sup> **increased inflammation (postinjection flare-up)**<sup>{R-15; 16}</sup>

#### Rabbits

**Hepatopathy**<sup>{R-20}</sup>

#### Sheep

**Appetite, decreased**;<sup>{R-76}</sup> **thyroid hormone metabolism alterations**—decreased plasma thyroxine;<sup>{R-168}</sup> **shedding of or slowed growth of wool**—the decrease in wool growth and the amount of shedding is dose-related<sup>{R-76; 168}</sup>

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

#### All species

**Hypoadrenocorticism, acute**<sup>{R-38}</sup> (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.<sup>{R-6; 27; 136}</sup>

### Human side/adverse effects<sup>{R-2}</sup>

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;**<sup>[R-30]</sup> **polyuria/polydipsia;**<sup>[R-1, 5, 14, 148]</sup> **sodium and fluid retention and potassium loss**—associated with medications that have mineralocorticoid effects<sup>[R-6]</sup>

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.

*Pharmacologic* 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.<sup>[R-30]</sup>

*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.<sup>[R-30; 136]</sup> 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.<sup>[R-30; 136]</sup> 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.<sup>[R-30]</sup> Alternate-day therapy can reduce adrenocortical suppression and decrease the effects of hyperadrenocorticism,<sup>[R-30; 136]</sup> but it will not completely prevent the eventual development of adverse effects.<sup>[R-136]</sup> Among other things, the susceptibility to urinary tract infections may not be decreased.<sup>[R-163]</sup> 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.<sup>{R-30; 136}</sup> 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 important strategy while treatment is ongoing. Tapering the dose is also important when discontinuing treatment.

It is unknown how much risk of iatrogenic secondary hypoadrenocorticism there is for an animal without a subsequent episode of stress.<sup>{R-136}</sup> Reports of iatrogenic acute adrenocortical insufficiency are rare in animals.<sup>{R-27}</sup> The possible suppression of adrenal function should be considered whenever glucocorticoid administration is discontinued and, if necessary, the dose should be tapered off to allow resumption of normal endogenous cortisol concentrations and avoid hypoadrenal crisis.<sup>{R-19}</sup> Many practitioners assume that therapy for more than 2 weeks requires a tapering of dose for withdrawal in dogs;<sup>{R-31; 136}</sup> however, the duration of adrenal recovery is highly variable among individual animals.<sup>{R-127}</sup> Animals that have been considered most at risk are those that are given greater than physiological replacement dosing for more than 2 weeks and that subsequently undergo sudden physiologic stress in the 6 weeks after therapy is discontinued.<sup>{R-27}</sup>

*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.

**Bases**—These are the glucocorticoids in their free alcohol or base form. Each has a slightly different structure affecting its glucocorticoid and mineralocorticoid activity and its duration of action. The bases have traditionally been divided into short, intermediate, and long duration.<sup>{R-34}</sup> a) short-acting—cortisone, hydrocortisone, b) intermediate-acting—prednisone, prednisolone, methylprednisolone, and triamcinolone, c) long-acting—dexamethasone and flumethasone.

**Esters or salts**—Esterification of a glucocorticoid affects its water and lipid solubility and the rate at which it is absorbed from the injection site.<sup>{R-30; 31}</sup>

**Acetate, diacetate, and tebutate esters**—Slow and sustained absorption from intramuscular depot injections.<sup>{R-30; 31}</sup> These are poorly water-soluble.

**Acetonide esters**—Slow and sustained absorption from intramuscular or subcutaneous depot injections.<sup>{R-30; 31}</sup> These are poorly water-soluble.

**Succinate and phosphate esters**—Rapid action from intravenous or intramuscular administration. These are the most water-soluble esters and are rapidly absorbed; their duration of action is similar to their corresponding base.<sup>{R-30}</sup>

The relative anti-inflammatory potencies of the glucocorticoid bases have been described based on four different irritant response tests in rats, with varying results.<sup>{R-38; 188}</sup> The relevance of these potencies to dose and efficacy in particular clinical situations can vary.

	Relative anti-inflammatory potency	Relative sodium-retaining potency*	Approximate duration of action (adrenal suppression) (hours)
Cortisol (hydrocortisone)	1	1	<12
Cortisone	0.8	0.8	<12

Prednisolone	4	0.8	12–36
Prednisone	4	0.8	12–36
Methylprednisolone	5	0–0.5	12–36
Triamcinolone <sup>(R-31)</sup>	3–5	0	24–48
Isoflupredone	17	0*	–
Betamethasone	25–30	0	>48
Dexamethasone	25–30	0	>48
Flumethasone	30	0	>48

\* Repeated high doses of some glucocorticoids with previously unreported mineralocorticoid effect may exacerbate electrolyte disturbances in susceptible animals.<sup>(R-214)</sup> One example is clinical hypokalemia reported in some ketotic, postparturient cattle treated with multiple high doses of isoflupredone, in combination with other medications.<sup>(R-214)</sup>

#### For intrasynovial administration

Product labeling recommends intrasynovial injection when it can help reduce or avoid systemic administration of corticosteroids or when systemic corticosteroids are contraindicated.<sup>(R-15; 16)</sup> Strict asepsis should be followed to minimize the risk of septic arthritis. Exercise should be restricted and repeated injections should be avoided<sup>(R-121-126)</sup> to reduce the risk of side effects.

#### Diet/Nutrition

When long-term glucocorticoid therapy is used, a protein-rich, potassium chloride-supplemented diet has been recommended to counteract nitrogen and potassium loss.<sup>(R-18)</sup>

## DEXAMETHASONE

### Summary of Differences

Laboratory value alterations: Dexamethasone can decrease serum testosterone in bulls and rams.<sup>(R-169; 170)</sup>

Lactation: Dexamethasone concentrations in milk have been measured in cattle.<sup>(R-71; 72)</sup>

Pharmacology/pharmacokinetics: Dexamethasone sodium phosphate is well-suited for rapid utilization when administered intravenously.<sup>(R-11)</sup>

Side/adverse effects: Dexamethasone has been associated with temporary sperm defects in cattle.<sup>(R-169)</sup>

Veterinary dosing information: In rats, dexamethasone has approximately 25 to 30 times the anti-inflammatory potency of cortisol and six to seven times the potency of prednisolone.<sup>(R-38)</sup> Dexamethasone has an insignificant amount of mineralocorticoid effect.<sup>(R-38)</sup>

### Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

#### DEXAMETHASONE ORAL POWDER

##### Usual dose:

Inflammation, including musculoskeletal inflammation—*Cattle and horses*: Oral, [0.04 to 0.15 mg per kg of body weight a day].<sup>(R-212)</sup>

Ketosis—*Cattle*: Oral, [0.01 to 0.04 mg per kg of body weight a day (5 to 20 mg total dose)].<sup>(R-5)</sup>

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. See also the *Withdrawal times* section below.

##### Strength(s) usually available:<sup>(R-13)</sup>

U.S.—

Veterinary-labeled product(s):<sup>(R-5)</sup>  
10 mg per 15 grams of powder (Rx) [*Azium Powder*].

Canada—

Veterinary-labeled product(s):<sup>(R-3)</sup>  
10 mg per 15 grams of powder (Rx) [*Azium Powder*];

*Dexone*; GENERIC].

**Withdrawal times:**

U.S. and Canada—Although dexamethasone oral powder is labeled for use in cattle, product labeling does not list an established meat or milk withdrawal time<sup>{R-3; 5}</sup> and the U.S. government has not established a safe level for dexamethasone in animal products for human consumption. However, if dexamethasone is administered to cattle at a dose of 0.04 to 0.07 mg per kg of body weight (20 to 30 mg total dose), there is some evidence to suggest that a withdrawal time of 96 hours for milk is necessary to avoid residues that would be considered potentially harmful by some national and international authorities.<sup>{R-21}</sup>

Currently, there are not enough data to estimate withdrawal times for meat for most dexamethasone formulations available in the U.S. and Canada. However, there is some evidence that a significant withdrawal is necessary. For this formulation, it is possible that if a dose of 0.06 mg per kg of body weight is administered to cattle, at least 4 days are necessary to clear muscle tissue of residues. Some data suggest longer withdrawals may be necessary to clear dexamethasone residues from other tissues. Pigs may clear all tissues of residues within 1 day of administration.<sup>{R-21}</sup>

Information is not available for residue depletion or human food safety if a dose higher than 0.07 mg per kg of body weight is administered to food-producing animals.

Note: Product labeling lists a total dose of 5 to 10 mg per animal (0.01 to 0.02 mg per kg of body weight) a day for cattle.<sup>{R-3; 5}</sup>

These products are not labeled for use in horses intended for food or in preruminating calves.<sup>{R-5; 22}</sup>

**Packaging and storage:** Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by the manufacturer.<sup>{R-19}</sup> Protect from light.<sup>{R-19}</sup>

**USP requirements:** Not in USP.<sup>{R-183}</sup>

**DEXAMETHASONE TABLETS USP**

**Usual dose:**

[Dermatoses];

Inflammation, general; or

[Inflammation, musculoskeletal]—*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.<sup>{R-212}</sup>

Note: [Induction of abortion]<sup>1</sup>—*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 twelve 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.<sup>{R-118}</sup>

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.<sup>{R-118}</sup> In 60% of dogs treated, lethargy and depression may be noted during the abortion period.<sup>{R-118}</sup>

**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):<sup>{R-2}</sup>

0.25 mg (250 mcg) (Rx) [*Decadron*; GENERIC].

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

0.75 mg (750 mcg) (Rx) [*Decadron; Hexadrol*; GENERIC].  
1 mg (Rx) [GENERIC].  
1.5 mg (Rx) [*Decadron; Hexadrol*; GENERIC].  
2 mg (Rx) [GENERIC].  
4 mg (Rx) [*Decadron; Hexadrol*; GENERIC].  
6 mg (Rx) [*Decadron*; GENERIC].

Canada—

Veterinary-labeled product(s):<sup>{R-12; 13}</sup>

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

Human-labeled product(s):<sup>{R-2}</sup>

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

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

4 mg (Rx) [*Dexasone*; 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.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

## DEXAMETHASONE INJECTION USP

### Usual dose:

Allergic disorders—

*Cats and dogs:* Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day.<sup>{R-212}</sup> This dose may be repeated every twenty-four hours for three to five days<sup>{R-4}</sup> 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].<sup>{R-212}</sup>

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.<sup>{R-4; 6}</sup> See also the *Withdrawal times* section below.

Dermatoses—*Cats and dogs:* Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day.<sup>{R-212}</sup> This dose may be repeated every twenty-four hours for three to five days<sup>{R-4}</sup> or as necessary for the disease condition.

Disk disease, intervertebral—*Dogs:* Intravenous, 0.07 to 0.15 mg per kg of body weight a day.<sup>{R-212}</sup>

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*).

Inflammation, including musculoskeletal and [ocular]<sup>1</sup>  
inflammation—

*Cats and dogs:* Intramuscular or intravenous, 0.07 to 0.15 mg per kg of body weight a day.<sup>{R-212}</sup> This dose may be repeated every twenty-four hours for three to five days<sup>{R-4}</sup> or as necessary for the disease condition.

*Cattle:* Intramuscular or intravenous, [0.04 to 0.15 mg per kg of body weight a day].<sup>{R-212}</sup>

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.<sup>{R-4; 6}</sup> See also the *Withdrawal times* section

below.

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

*Ketosis—Cattle:* Intramuscular or intravenous, 0.01 to 0.04 mg per kg of body weight (5 to 20 mg total dose) a day.<sup>{R-4; 6}</sup> See also the *Withdrawal times* section below.

[Abortion, induction of]<sup>1</sup>—*Cattle:* Intramuscular, 0.05 mg per kg of body weight (approximately 25 mg as a total dose), administered after the 100th day of gestation, usually in conjunction with a prostaglandin.<sup>{R-190; 191}</sup> The risk of fetal mummification, retained placenta, metritis, or dystocia should be considered.<sup>{R-191}</sup> See also the *Withdrawal times* section below.

[Hyperadrenocorticism (diagnosis)]<sup>1</sup>—

*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.<sup>{R-140; 177}</sup> Blood cortisol samples are taken at four and eight hours postinjection.<sup>{R-64}</sup> Normal adrenocortical suppression is typically defined as < 1.4 mcg of cortisol per decaliter at eight hours.<sup>{R-140}</sup>

Note: The above test dose is based on a study establishing suppression of endogenous cortisol in normal cats in response to dexamethasone administration.<sup>{R-140}</sup>

Although insufficient data are available to confirm the accuracy of the *high-dose dexamethasone suppression test* in cats, some clinicians have used the following regimen: After a baseline blood cortisol sample is taken, an intravenous bolus of 1 mg per kg of body weight is administered as a single dose.<sup>{R-140; 177}</sup> Blood cortisol samples are taken at four and eight hours postinjection.<sup>{R-64}</sup> Plasma cortisol < 50% of baseline concentration at four or eight hours postinjection or plasma cortisol < 1.4 mcg/decaliter at four or eight hours may be an indication of pituitary-dependent hyperadrenocorticism;<sup>{R-177}</sup> however, specific values may vary depending on the laboratory. A lack of cortisol suppression sufficient to meet the criteria is presumed to indicate an adrenal tumor.

*Dogs:*

Low-dose dexamethasone suppression test—After a baseline blood cortisol sample is taken, an intravenous bolus of 0.01 mg per kg of body weight is administered as a single dose.<sup>{R-58-60}</sup> Blood cortisol samples are taken at four and eight hours postinjection.<sup>{R-64}</sup> Normal adrenocortical suppression is typically defined as < 1.4 mcg of cortisol per decaliter at eight hours.<sup>{R-58; 62-64}</sup> For dogs that show evidence of hyperadrenocorticism by a cortisol concentration of ≥ 1.4 mcg/decaliter at eight hours, a plasma cortisol < 50% of baseline concentration at four or eight hours postinjection or plasma cortisol < 1.4 mcg/decaliter at four hours is a strong indication of pituitary-dependent hyperadrenocorticism;<sup>{R-64}</sup> however, specific values may vary depending on the laboratory.

High-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.<sup>{R-64}</sup> Blood cortisol samples are taken at four and eight hours postinjection.<sup>{R-64}</sup> Plasma cortisol < 50% of baseline concentration at four or eight hours postinjection or plasma cortisol < 1.4 mcg per decaliter at four or eight hours is a strong indication of pituitary-dependent hyperadrenocorticism;<sup>{R-64}</sup> however, specific values may vary depending on the laboratory. A lack of cortisol suppression sufficient to meet the criteria is presumed to indicate an adrenal tumor.

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 injection of 0.04

mg per kg of body weight is administered.<sup>{R-179}</sup> A blood cortisol sample is taken nineteen to twenty-four hours postinjection.<sup>{R-177; 179}</sup> Normal adrenocortical suppression is typically defined as less than 1 mcg of cortisol per decaliter at twenty to twenty-four hours.<sup>{R-179}</sup>

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

[Parturition induction]<sup>1</sup>—

*Cattle:* Intramuscular, 0.05 mg per kg of body weight (approximately 25 mg total dose per animal), given as a single dose in the last week to two weeks of gestation<sup>{R-110; 112; 190; 191}</sup> and administered concurrently with an intramuscular dose of a prostaglandin (PGF<sub>2alpha</sub>), such as cloprostenol at a total dose of 0.5 mg per animal.<sup>{R-110; 112}</sup> See also the *Withdrawal times* section below.

Note: It has been suggested that the likelihood of accurate prediction of the time of parturition may be increased and the risk of some side effects, such as retained placenta, may be decreased by pretreatment administration of a relatively long-acting corticosteroid approximately one week before induction.<sup>{R-110; 112}</sup> Triamcinolone at an intramuscular dose of 0.016 mg per kg of body weight has been used for pretreatment in the induction of parturition;<sup>{R-110}</sup> however, there is some risk that the pretreatment itself will induce early parturition before induction.

*Sheep:* Intramuscular, 0.15 mg per kg of body weight (10 mg total dose) a day for one to five days, administered in the last week of gestation.<sup>{R-116; 172}</sup> See also the *Withdrawal times* section below.

Note: [Edema associated with brain tumors (see *Inflammation, neurologic* in the *Indications* section of this monograph)]<sup>1</sup>— 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.<sup>{R-219}</sup> However, it should be emphasized that corticosteroids have not been shown to be effective in trauma-induced cerebral edema,<sup>{R-220}</sup> although they may be of benefit in reducing tissue damage mediated by mechanisms other than cerebral edema.<sup>{R-223}</sup>

[Anemia, immune-mediated hemolytic]<sup>1</sup>—*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.

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-4; 6}</sup>  
2 mg per mL (Rx) [*Azium Solution; Dexaject; Dexasone; Dexazone 2 mg; GENERIC*].

Canada—

Veterinary-labeled product(s):<sup>{R-181; 184}</sup>  
2 mg per mL (Rx) [*Rafter Dex*].

**Withdrawal times:**

U.S. and Canada—Although dexamethasone injection is labeled for use in cattle, product labeling does not list an established meat or milk withdrawal time<sup>{R-4; 181}</sup> and the U.S. government has not established a safe level for dexamethasone in animal products for human consumption. However, if dexamethasone is administered to cattle at a dose of 0.04 to 0.07 mg per kg of body weight (20 to 30 mg total dose), there is some evidence to suggest that a withdrawal time of 96 hours for milk is necessary to avoid residues that would be considered potentially harmful by some national and international authorities.<sup>{R-21}</sup>



Currently, there are not enough data to estimate withdrawal times for meat for most dexamethasone formulations available in the U.S. and Canada. However, there is some evidence that a significant withdrawal is necessary. For this formulation, it is possible that if a dose of 0.06 mg per kg of body weight is administered to cattle, at least 4 to 8 days are necessary to clear muscle tissue of residues. The rate at which this formulation clears other tissues is unknown, but other formulations available in Europe have shown that at least 3 weeks for liver and kidney tissues and up to 6 weeks for the injection site are necessary for residues to fall within generally accepted standards. In the same situation for pigs, residues may fall more rapidly in liver and kidney tissues.<sup>{R-21}</sup> Information is not available for residue depletion or human food safety if a dose higher than 0.07 mg per kg of body weight is administered to food-producing animals.

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.<sup>{R-4; 6; 13}</sup>

These products are not labeled for use in horses intended for food or in prerinuating calves to be processed for veal.<sup>{R-4}</sup>

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

**USP requirements:** Preserve in light-resistant single-dose or multiple-dose containers, preferably of Type I glass. A sterile solution of Dexamethasone in Water for Injection. Label it to indicate that it is for veterinary use only. Contains the labeled amount, within ±10%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, pH (4.0–5.5), and Particulate matter, and for Injections.<sup>{R-183}</sup>

## DEXAMETHASONE 21 PHOSPHATE INJECTION

### Usual dose:

[Inflammation, musculoskeletal]—*Cattle and horses:* Intramuscular or intravenous, 0.04 to 0.15 mg per kg of body weight as an initial dose, followed by the same dose every twenty-four hours, as necessary for the disease condition.<sup>{R-212}</sup> See also the *Withdrawal times* section below.

[Ketosis]—*Cattle:* Intramuscular or intravenous, 0.02 to 0.04 mg per kg of body weight as an initial dose, followed by the same dose every twenty-four hours, as necessary for the disease condition.<sup>{R-1}</sup> See also the *Withdrawal times* section below.

### Strength(s) available:<sup>{R-13}</sup>

U.S.—

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

Canada—

Veterinary-labeled product(s):  
5 mg per mL (OTC) [GENERIC].

### Withdrawal times:

U.S. and Canada—Dexamethasone 21 phosphate injection is not labeled for use in animals in the U.S.; therefore, withdrawal times have not been established, and the U.S. government has not established a safe level for dexamethasone in animal products for human consumption. Although dexamethasone 21 phosphate injection is labeled for use in cattle in Canada, product labeling does not list an established meat or milk withdrawal time.<sup>{R-1}</sup> However, if dexamethasone is administered to cattle at a dose of 0.04 to 0.07 mg per kg of body weight (20 to 30 mg total dose), there is some evidence to suggest that a withdrawal time of 96 hours for milk is necessary to avoid residues that would be considered potentially harmful by some national and international authorities.<sup>{R-21}</sup>

Currently, there are not enough data to estimate withdrawal times for meat for most dexamethasone formulations available in the U.S. and Canada. However, there is some evidence that a significant withdrawal is necessary. For this formulation, it is

possible that if a dose of 0.06 mg per kg of body weight is administered to cattle, at least 4 to 8 days are necessary to clear muscle tissue of residues. The rate at which this formulation clears other tissues is unknown, but other formulations available in Europe have shown that at least 3 weeks for liver and kidney tissues and up to 6 weeks for the injection site are necessary for residues to fall within generally accepted standards. In the same situation for pigs, residues may fall more rapidly in liver and kidney tissues.<sup>(R-21)</sup> Information is not available for residue depletion or human food safety if a dose higher than 0.07 mg per kg of body weight is administered to food-producing animals.

Note: Canadian product labeling lists a total dose of 0.02 to 0.04 mg per kg of body weight (about 10 to 20 mg per animal) for cattle.<sup>(R-1)</sup>

**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.<sup>(R-1)</sup>

**USP requirements:** Not in USP.<sup>(R-183)</sup>

## 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]:* Intravenous, 0.07 to 0.15 mg (base) per kg of body weight a day. The dose may be repeated daily if necessary.

*[Cattle]:* 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>1</sup>—*Cats and dogs:* See *Dexamethasone Injection*.

[Ketosis]—*Cattle:* Intramuscular or intravenous, 0.01 to 0.04 mg (base) per kg of body weight (5 to 20 mg total dose) a day.<sup>(R-176)</sup> See also the *Withdrawal times* section below.

[Septic shock]<sup>1</sup>—*Cats, cattle, dogs, horses and pigs:* Intravenous, 0.5 to 5 mg (base) per kg of body weight.<sup>(R-212)</sup> See also the *Withdrawal times* section below.

### Strength(s) usually available:<sup>(R-13)</sup>

U.S.—

Veterinary-labeled product(s):<sup>(R-11)</sup>

3.33 mg per mL (base; equivalent to 4 mg per mL sodium phosphate salt) (Rx) [*Dexaject SP*; GENERIC].

Canada—

Veterinary-labeled product(s):<sup>(R-176)</sup>

1.67 mg (base; equivalent to 2 mg sodium phosphate salt) per mL (OTC) [*Dexamethasone 2*; GENERIC].

4.16 mg (base; equivalent to 5 mg sodium phosphate salt) per mL (OTC) [*Dexamethasone 5; Uni-Dex*].

### Withdrawal times:

U.S. and Canada—Dexamethasone sodium phosphate injection is not labeled for use in food-producing animals in the U.S.; therefore, withdrawal times have not been established<sup>(R-11)</sup> and the U.S. government has not established a safe level for dexamethasone in animal products for human consumption. Although dexamethasone sodium phosphate is labeled for use in cattle in

Canada, product labeling does not list an established meat or milk withdrawal time.<sup>{R-176}</sup> However, if dexamethasone is administered to cattle at a dose of 0.04 to 0.07 mg per kg of body weight (20 to 30 mg total dose), there is some evidence to suggest that a withdrawal time of 96 hours for milk is necessary to avoid residues that would be considered potentially harmful by some national and international authorities.<sup>{R-21}</sup>

Currently, there are not enough data to estimate withdrawal times for meat for most dexamethasone formulations available in the U.S. and Canada. However, there is some evidence that a significant withdrawal is necessary. For this formulation, it is possible that if a dose of 0.06 mg per kg of body weight is administered to cattle, at least 4 days are necessary to clear muscle tissue of residues. Some data suggest longer withdrawals may be necessary to clear dexamethasone residues from other tissues. Pigs may clear all tissues of residues within 1 day of administration.<sup>{R-21}</sup> Information is not available for residue depletion or human food safety if a dose higher than 0.07 mg per kg of body weight is administered to food-producing animals.

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.<sup>{R-176}</sup>

These products are not labeled for use in horses intended for food.<sup>{R-176}</sup>

**Packaging and storage:** Store between 15 and 30 °C (59 and 86 °F),<sup>{R-11}</sup> unless otherwise specified by the manufacturer. Protect from light. Protect from freezing.

**USP requirements:** Preserve in single-dose or in 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. Meets the requirements for Identification, Bacterial endotoxins, and pH (7.0–8.5), and for Injections.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in the U.S.

## ***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: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### **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.<sup>{R-18; 185}</sup>

*Horses*<sup>1</sup>: Intramuscular or intravenous, 1.25 to 2.5 mg per animal, as a single dose. If necessary, the dose may be repeated.<sup>{R-18}</sup>

[Cats]<sup>1</sup>: 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.<sup>{R-18; 185}</sup>

**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.<sup>{R-18; 185}</sup>

*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.<sup>{R-18; 185}</sup>

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.<sup>{R-18; 185}</sup>

**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.<sup>{R-18; 185}</sup>

*Horses*: Intramuscular or intravenous, 1.25 to 2.5 mg per animal, as a single dose. If necessary, the dose may be repeated.<sup>{R-18}</sup>

[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.<sup>{R-185}</sup>

[Cattle]: Canadian product labeling lists an intramuscular or intravenous dose of 1.25 to 5 mg a day per animal as a single dose.<sup>{R-185}</sup> If necessary, the dose may be repeated.<sup>{R-185}</sup>

**Inflammation, musculoskeletal (joint)<sup>1</sup>—**

*Dogs*: Intra-articular, 0.166 to 1 mg per animal, as a single dose.<sup>{R-18}</sup>

*Horses*: Intra-articular, 1.25 to 2.5 mg per animal, as a single dose.<sup>{R-18}</sup>

[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.<sup>{R-185}</sup> If necessary, the dose may be repeated.<sup>{R-185}</sup>

Note: The use of a microsyringe or standard tuberculin syringe may be helpful in accurately administering small amounts of flumethasone.<sup>{R-18}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—<sup>{R-18}</sup>

Veterinary-labeled product(s):  
0.5 mg per mL (Rx) [*Flucort*].

Canada—<sup>{R-185}</sup>

Veterinary-labeled product(s):  
0.5 mg per mL (OTC) [*Flucort*].

**Withdrawal times:**

U.S.—This product is not labeled for use in food-producing animals in the U.S.; therefore there are no established withdrawal times.

Canada—<sup>{R-185}</sup>

Species	Withdrawal time
	Meat (days)
<i>Cattle</i>	4

**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.

**USP requirements:** Not in USP.<sup>{R-183}</sup>

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

**HYDROCORTISONE**

**Summary of Differences**

Indications: Hydrocortisone is indicated in the treatment of adrenocortical

insufficiency.

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

### Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

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

### HYDROCORTISONE TABLETS USP

**Usual dose:** [Adrenocortical insufficiency]<sup>1</sup>—*Cats and dogs:* Oral, 1 to 2 mg per kg of body weight a day as an initial dose. Maintenance dose is determined based on patient response.

Note: Generally, other mineralocorticoids and glucocorticoids are preferred over hydrocortisone<sup>{R-223}</sup> in the treatment of adrenocortical insufficiency.

#### Strength(s) usually available:

U.S.—

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

Human-labeled product(s):<sup>{R-2}</sup>  
5 mg (Rx) [*Cortef*].  
10 mg (Rx) [*Cortef*; *Hydrocortone*; GENERIC].  
20 mg (Rx) [*Cortef*; *Hydrocortone*; GENERIC].

Canada—

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

Human-labeled product(s):<sup>{R-2}</sup>  
10 mg (Rx) [*Cortef*].  
20 mg (Rx) [*Cortef*].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). 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 30 minutes in water, in Apparatus 2 at 50 rpm), and Uniformity of dosage units.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

### ISOFLUPREDONE

#### Summary of Differences

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

#### Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### ISOFLUPREDONE ACETATE INJECTABLE SUSPENSION

#### Usual dose:

Allergic disorders;  
Inflammation, musculoskeletal; or  
Inflammation, ocular—

*Cattle:* Intramuscular, 10 to 20 mg as a total single dose per

animal.<sup>{R-23; 24}</sup> The dose may be repeated in twelve to twenty-four hours.<sup>{R-23; 24}</sup>

*Horses:* Intramuscular, 5 to 20 mg as a total single dose per animal.<sup>{R-23; 24}</sup> The dose may be repeated in twelve to twenty-four hours, as necessary.

*Pigs:* Intramuscular, 0.036 mg per kg of body weight.<sup>{R-23; 24}</sup>

Inflammation, musculoskeletal (joint)—*Horses:* Intrasynovial, 5 to 20 mg or more, as a total single dose per animal, depending on the size of the cavity.<sup>{R-23; 24}</sup>

Ketosis—*Cattle:* Intramuscular, 10 to 20 mg as a total single dose per animal.<sup>{R-23}</sup> The dose may be repeated in twelve to twenty-four hours.<sup>{R-23; 24}</sup> The high end of the dose is recommended as an initial dose, rather than repeating smaller doses.<sup>{R-23; 24}</sup>

Note: Repeating large doses of isoflupredone outside of label directions may lead to hypokalemia in some cattle.<sup>{R-214}</sup>

Note: [Chronic obstructive pulmonary disease]<sup>1</sup>—*Horses:* Although the safety and efficacy have not been established in the treatment of chronic obstructive pulmonary disease in horses, a total intramuscular dose of 10 to 14 mg (approximately 0.02 to 0.03 mg per kg of body weight), administered every twenty-four hours for five days, may be effective in the relief of signs.<sup>{R-26; 32}</sup> The dose may then be tapered off over a period of 10 to 20 days.<sup>{R-26}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-24}</sup>  
2 mg per mL (Rx) [*Predef 2X*].

Canada—

Veterinary-labeled product(s):<sup>{R-23}</sup>  
2 mg per mL (Rx) [*Predef 2X*].

**Withdrawal times:**

U.S.—<sup>{R-24}</sup>

Species	Withdrawal time	
	Meat (days)	
<i>Cattle, pigs</i>	7	

Note: This product is not labeled for use in preruminating calves intended to be processed for veal.<sup>{R-24}</sup>

Canada—<sup>{R-23}</sup>

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cattle</i>	5	72
<i>Pigs</i>	5	

**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.<sup>{R-23}</sup>

**USP requirements:** Not in USP.<sup>{R-183}</sup>

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

**METHYLPREDNISOLONE**

**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.<sup>{R-16; 38}</sup> It has approximately one half the sodium-retaining effect of cortisol in mice.<sup>{R-38}</sup>

## Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### METHYLPREDNISOLONE TABLETS USP

#### Usual dose:

Adrenocortical insufficiency, acute<sup>1</sup>—*Cats and dogs*: Oral, 0.1 to 0.25 mg per kg of body weight a day.<sup>{R-193; 206; 211}</sup>

Allergic disorders<sup>1</sup>;

Dermatoses<sup>1</sup>; or

Inflammation, including ocular and musculoskeletal inflammation<sup>1</sup>—*Cats and dogs*: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.<sup>{R-14}</sup>

Asthma<sup>1</sup>—*Cats*: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.<sup>{R-14}</sup>

Colitis, ulcerative<sup>1</sup>—*Dogs*: Oral, 0.05 to 0.45 mg per kg of body weight every twelve hours.<sup>{R-14}</sup>

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.<sup>{R-14}</sup>

[Disk disease, intervertebral]<sup>1</sup>—*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 *Methylprednisolone Sodium Succinate For Injection USP*).

[Lupus erythematosus]<sup>1</sup>—*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.<sup>{R-98; 99}</sup>

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

#### Strength(s) usually available:<sup>{R-13}</sup>

U.S.—<sup>{R-14; 192}</sup>

Veterinary-labeled product(s):

2 mg (Rx) [GENERIC].

4 mg (Rx) [*Medrol*].

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  $\pm 7.5\%$ . Meet the requirements for Identification, Dissolution (70% in 30 minutes in water in Apparatus 2 at 50 rpm), and Uniformity of dosage units.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for

products not commercially available in the U.S.

## 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<sup>{R-15}</sup> to six months apart.<sup>{R-31}</sup> The average total dose administered is 10 mg.<sup>{R-15}</sup>

*Dogs:* Intramuscular, 2 to 120 mg as a single total dose<sup>{R-15}</sup> (1.1 mg per kg of body weight<sup>{R-31}</sup>). The average total dose administered is 20 mg.<sup>{R-15}</sup>

Asthma—*Cats:* Intramuscular, 10 to 20 mg as a total dose administered at an interval from one week to six months apart.<sup>{R-15}</sup>

Inflammation, including musculoskeletal inflammation—

*Cats:* Intramuscular, 10 to 20 mg as a total dose, administered at an interval from one week<sup>{R-15}</sup> to six months apart.<sup>{R-31}</sup> The average total dose administered is 10 mg.<sup>{R-15}</sup>

*Dogs:* Intramuscular, 2 to 120 mg as a single total dose<sup>{R-15}</sup> (1.1 mg per kg of body weight<sup>{R-31}</sup>). The average total dose administered is 20 mg.<sup>{R-15}</sup>

*Horses:* Intramuscular, 200 mg as a single total dose.<sup>{R-15}</sup>

Inflammation, musculoskeletal (joint)—

*Dogs:* Intrasynovial, 20 mg as a single total dose for large synovial spaces.<sup>{R-15}</sup> The dose is decreased as the size of the joint space decreases.<sup>{R-15}</sup>

*Horses:* Intrasynovial, 40 to 240 mg as a single total dose.<sup>{R-15}</sup> The average dose is 120 mg.<sup>{R-15}</sup> The dose is decreased as the size of the joint space decreases.<sup>{R-15}</sup>

### Strength(s) usually available:<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-15}</sup>  
20 mg per mL (Rx) [*Depo-Medrol*].  
40 mg per mL (Rx) [*Depo-Medrol*].

Canada—

Veterinary-labeled product(s):<sup>{R-16; 17}</sup>  
20 mg per mL (OTC) [*Depo-Medrol*].  
40 mg per mL (OTC) [*Depo-Medrol*; *Methysone 40*;  
*Unimed*; *Vetacortyl*].

### Withdrawal times:

U.S. and Canada—Methylprednisolone acetate injectable suspension is not labeled for use in horses intended for food production.<sup>{R-16; 17}</sup>

**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.

**USP requirements:** Preserve in single-dose or in multiple-dose containers, preferably of Type I glass. A sterile suspension of Methylprednisolone Acetate in a suitable aqueous medium. Contains the labeled amount, within ±10%. Meets the requirements for Identification, Uniformity of dosage units, pH (3.0–7.0), and Particle size (not less than 99% are less than 20 micrometers in length [measured on longest axis] and not less than 75% are less than 10 micrometers in length, using 400x magnification), and for Injections.<sup>{R-183}</sup>

## 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]<sup>1</sup>—*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.<sup>{R-44}</sup>

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.<sup>{R-223}</sup>

**Size(s) usually available:**

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):<sup>{R-2; 186}</sup>

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

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

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

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

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

Canada—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):<sup>{R-2}</sup>

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.<sup>{R-186}</sup>

**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 units, and Labeling under Injections.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## **PREDNISOLONE**

### **Summary of Differences**

Pharmacology/pharmacokinetics: Prednisolone sodium succinate<sup>{R-7}</sup> 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.<sup>{R-16; 38}</sup> It has approximately 0.8 times the sodium-retaining effect of cortisol.<sup>{R-38}</sup>

## Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### PREDNISOLONE TABLETS USP

#### Usual dose:

Adrenocortical insufficiency, acute<sup>1</sup>—

*Dogs* and [*Cats*]: Oral, 0.2 mg per kg of body weight a day.<sup>{R-100; 195; 196}</sup> 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.<sup>{R-195}</sup> The dose is used in combination with mineralocorticoid replacement or alone in the treatment of secondary hypoadrenocorticism.<sup>{R-195}</sup>  
[*Horses*]: Oral, 0.1 to 0.5 mg per kg of body weight a day.<sup>{R-210; 211}</sup>

Allergic disorders<sup>1</sup>; or

Dermatoses<sup>1</sup>—*Dogs* and [*Cats*]: Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>{R-8}</sup> 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.<sup>{R-8; 100; 193}</sup>

Inflammation, including ocular and musculoskeletal inflammation<sup>1</sup>—

*Dogs*: Oral, 0.5 to 1 mg per kg of body weight every twenty-four hours as an initial dose.<sup>{R-8}</sup> 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.

[*Cats*]: Oral, 2.2 mg per kg of body weight every twenty-four hours as an initial dose.<sup>{R-28; 31; 100; 189}</sup> 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.

Ulcerative colitis<sup>1</sup>—*Dogs*: Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>{R-8}</sup> 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.

[Anemia, autoimmune, hemolytic]<sup>1</sup>—*Cats* and *dogs*: Oral, 1 to 3 mg per kg of body weight every twelve to twenty-four hours.<sup>{R-39-41; 94; 98; 99}</sup> 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.<sup>{R-38}</sup>

[Asthma]<sup>1</sup>—*Cats*: Oral, 2.2 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>{R-28; 31; 100; 189}</sup> 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.

[Disk disease, intervertebral]<sup>1</sup>—*Dogs*: Oral, 0.5 to 1 mg per kg of body weight every twenty-four hours as an initial dose. 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.

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*).

[Lupus erythematosus]<sup>1</sup>—*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.<sup>{R-98; 99}</sup>

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

[Lymphoma]<sup>1</sup>—*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.<sup>{R-83-86; 100; 108}</sup>

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.

[Mast cell tumors]<sup>1</sup>—*Dogs*: Oral, 1 mg per kg of body weight every twenty-four hours.<sup>{R-100; 107}</sup>

[Pemphigoid]<sup>1</sup>; or

[Pemphigus]<sup>1</sup>—*Dogs*: Oral, 2 to 3 mg per kg of body weight every twelve hours.<sup>{R-39-41}</sup> 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.<sup>{R-39-41}</sup>

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

[Pemphigus]<sup>1</sup>—*Cats*: Oral, 2 to 3 mg per kg of body weight every twelve hours.<sup>{R-39-41}</sup> 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.<sup>{R-39-41}</sup>

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

[Thrombocytopenia, immune-mediated]<sup>1</sup>—*Dogs*: Oral, 2 mg per kg of body weight every twelve hours for seven to fourteen days.<sup>{R-94}</sup>

Note: In some cases that are refractory to treatment, other immunosuppressants, such as azathioprine or cyclophosphamide, are added to this regimen;<sup>{R-94}</sup> however, it is controversial whether the combined therapy improves survival.

The above dose is based on retrospective studies.

Note: [Chronic obstructive pulmonary disease]<sup>1</sup>—*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.<sup>{R-26; 32}</sup> The dose should be tapered and, when feasible, discontinued.<sup>{R-26}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-8; 187}</sup>

5 mg (Rx) [*PrednisTab*].

20 mg (Rx) [*PrednisTab*].

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 well-closed container.

**USP requirements:** Preserve in well-closed containers. Contain the labeled amount, within ±10%. Meet the requirements for Identification, Dissolution (70% in 30 minutes in water in Apparatus 2 at 50 rpm), and Uniformity of dosage units.<sup>{R-183}</sup>

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### PREDNISOLONE ACETATE INJECTABLE SUSPENSION USP

#### Usual dose:

[Dermatoses]—*Dogs*: Intramuscular, 10 to 30 mg as a total dose per animal.<sup>{R-10}</sup>

[Inflammation, musculoskeletal]—

*Dogs*: Intramuscular, 10 to 30 mg as a total dose per animal.<sup>{R-10}</sup>

*Horses*: Intramuscular, 100 to 200 mg as a total dose per animal.<sup>{R-10}</sup>

[Ketosis]—*Cattle*: Intramuscular, 100 to 200 mg as a total dose per animal.<sup>{R-10}</sup>

#### Strength(s) usually available:<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Canada—

Veterinary-labeled product(s):<sup>{R-10}</sup>

10 mg per mL (OTC) [GENERIC].

50 mg per mL [*Uni-Pred 50*; GENERIC].

#### Withdrawal times:

U.S.—This product is not labeled for use in food-producing animals in the U.S.; therefore, there are no established withdrawal times.

Canada—<sup>{R-10}</sup>

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cattle</i>	5	72

**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.<sup>{R-10}</sup>

**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.<sup>{R-183}</sup>

### PREDNISOLONE SODIUM SUCCINATE FOR INJECTION USP

#### Usual dose:

Adrenocortical insufficiency, acute—*Cats* and *dogs*: Intramuscular or intravenous, 1 to 2 mg per kg of body weight as an initial dose,<sup>{R-193}</sup> followed by equal maintenance doses at one-, three-, six-, or ten-hour intervals.<sup>{R-7; 9}</sup> The intravenous dose should be administered slowly.<sup>{R-7}</sup>

Allergic disorders; or

Inflammation, including ocular and musculoskeletal inflammation

*Cats*: Intramuscular, 1 mg per kg of body weight.<sup>{R-9}</sup> The dose may be repeated in twelve to twenty-four hours and continued for three to five days, if necessary.<sup>{R-7}</sup>

*Dogs*: Intramuscular, 0.5 to 1 mg per kg of body weight.<sup>{R-9; 193}</sup>

The dose is repeated in twelve to twenty-four hours and continued for three to five days.<sup>{R-7}</sup>

*Horses*: Intramuscular or intravenous, 0.25 to 1 mg per kg of body weight.<sup>{R-9}</sup> If administered intravenously, the dose should be given slowly over thirty seconds to one minute.<sup>{R-7}</sup>

The dose should be repeated at twelve, twenty-four, or forty-eight hours, depending on clinical response.<sup>{R-9}</sup>

**Dermatoses—**

*Cats:* Intramuscular, 1 mg per kg of body weight.<sup>{R-9}</sup> The dose may be repeated in twelve to twenty-four hours and continued for three to five days, if necessary.<sup>{R-7}</sup>

*Dogs:* Intramuscular, 0.5 to 1 mg per kg of body weight.<sup>{R-9; 193}</sup> The dose is repeated in twelve to twenty-four hours and continued for three to five days.<sup>{R-7}</sup>

**Septic shock—**

*Cats, dogs, and horses:* Intravenous, 15 to 30 mg per kg of body weight as an initial dose,<sup>{R-193}</sup> to be repeated in 4 to 6 hours.<sup>{R-54-56}</sup> The intravenous dose should be administered slowly.<sup>{R-9}</sup>

Note: This treatment regimen should be administered with aggressive fluid therapy.

Note: [Immunosuppression]<sup>1</sup>—*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<sup>{R-9}</sup> has been used for immunosuppression. The dose is then tapered to 2 to 4 mg per kg of body weight every forty-eight hours.<sup>{R-189}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup> (When mixed according to manufacturer's instructions)—

**U.S.:**

Veterinary-labeled product(s)—<sup>{R-7}</sup>  
10 mg per mL (Rx) [*Solu-Delta-Cortef*].  
50 mg per mL (Rx) [*Solu-Delta-Cortef*].

**Canada:**

Veterinary-labeled product(s)—<sup>{R-9}</sup>  
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.<sup>{R-7}</sup> any unused reconstituted product should be discarded.<sup>{R-7}</sup> If the solution becomes cloudy after reconstitution, it should not be used intravenously.<sup>{R-7}</sup>

**Incompatibilities:** Prednisolone sodium succinate should not be added to calcium infusion solutions.<sup>{R-7}</sup>

**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.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## **PREDNISONONE**

### **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<sup>(R-100)</sup> 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.<sup>(R-16; 38)</sup> It has approximately 0.8 times the sodium-retaining effect of cortisol in mice.<sup>(R-38)</sup>

## Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

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

## PREDNISONE TABLETS USP

### Usual dose:

[Adrenocortical insufficiency]<sup>1</sup>—

*Cats and dogs:* Oral, 0.2 mg per kg of body weight a day.<sup>(R-100; 195;</sup>

<sup>196)</sup> 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.<sup>(R-195)</sup> The dose is used in combination with mineralocorticoid replacement therapy or alone in the treatment of secondary hypoadrenocorticism.<sup>(R-195)</sup>

*Horses:* Oral, 0.1 to 0.5 mg per kg of body weight a day.<sup>(R-100; 210; 211)</sup>

[Allergic disorders];

[Dermatoses]; or

[Inflammation], including ocular<sup>1</sup> and musculoskeletal inflammation—

*Cats:* Oral, 2.2 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>(R-31; 189)</sup> Once clinical effect is achieved, the dose should be tapered to reach an effective alternate-day dose administered every forty-eight hours.

*Dogs:* Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>(R-31; 189)</sup> Once clinical effect is achieved, the dose should be tapered to reach an effective alternate-day dose administered every forty-eight hours.

[Anemia, autoimmune, hemolytic]<sup>1</sup>—*Cats and dogs:* Oral, 1 to 3 mg per kg of body weight every twelve to twenty-four hours.<sup>(R-39-41; 94; 98; 99)</sup> Treatment is continued until the disease is controlled and, when clinically possible, then 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.<sup>(R-38)</sup>

[Asthma]<sup>1</sup>—*Cats:* Oral, 2.2 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>(R-28; 31; 189)</sup> Once clinical effect is achieved, the dose should be tapered to reach an effective alternate-day dose administered every forty-eight hours.

[Disk disease, intervertebral]<sup>1</sup>—*Dogs:* Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>(R-31; 189)</sup> Once clinical effect is achieved, the dose should be tapered to reach an effective alternate-day dose administered every forty-eight 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 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*).

[Lupus erythematosus]<sup>1</sup>—*Dogs:* Oral, 1 to 1.5 mg per kg of body weight every twelve hours or 2 to 3 mg every twenty-four hours for two weeks.<sup>(R-98; 99)</sup> With a good response to treatment two weeks after initiation, the dose should be halved, and four weeks after initiation the dosing interval should be doubled to forty-eight hours and the response monitored.

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

[Lymphoma]<sup>1</sup>—*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.<sup>{R-83-86; 100; 108}</sup>

It is very uncommon for prednisone to be administered as a sole agent because combination chemotherapy is often much more effective and use of prednisone alone is thought to make lymphoma less responsive to subsequent chemotherapy. The particular combination therapeutic regimen is chosen based on the animal's initial evaluation and cancer staging followed by subsequent evaluations.

[Mast cell tumors]<sup>1</sup>—*Dogs*: Oral, 1 mg per kg of body weight every twenty-four hours.<sup>{R-107}</sup>

[Pemphigoid]<sup>1</sup>—*Dogs*: Oral, 2 to 3 mg per kg of body weight every twelve hours.<sup>{R-39-41; 100}</sup> 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.<sup>{R-39-41}</sup>

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

[Pemphigus]<sup>1</sup>—*Cats and dogs*: Oral, 2 to 3 mg per kg of body weight every twelve hours.<sup>{R-39-41}</sup> After symptoms have been controlled, a maintenance dose of 2 mg per kg of body weight for cats and 1 to 2 mg per kg of body weight for dogs, 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.<sup>{R-39-41}</sup>

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

[Thrombocytopenia, immune-mediated]<sup>1</sup>—*Dogs*: Oral, 2 mg per kg of body weight every twelve hours for seven to fourteen days.<sup>{R-94; 100}</sup>

Note: The above dose is based on retrospective studies. In some cases that are refractory to treatment, more potent immunosuppressants, such as azathioprine or cyclophosphamide, are added to this regimen.<sup>{R-94}</sup>

[Ulcerative colitis]<sup>1</sup>—*Dogs*: Oral, 0.5 to 1 mg per kg of body weight every twelve to twenty-four hours as an initial dose.<sup>{R-8}</sup> Once clinical effect is achieved, the dose should be tapered to reach an effective alternate-day dose administered every forty-eight hours.

Note: [Chronic obstructive pulmonary disease]<sup>1</sup>—*Horses*: Although the safety and efficacy have not been established, a 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.<sup>{R-26; 32}</sup> The dose should be tapered and, when feasible, discontinued.<sup>{R-26}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—

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

Canada—

Veterinary-labeled product(s):<sup>{R-28}</sup>  
5 mg (Rx) [*Predsonex-5*].

**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 (80% in 30 minutes in water in Apparatus 2 at 50 rpm), and Uniformity of dosage units.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## 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

#### TRIAMCINOLONE TABLETS USP

##### Usual dose:

Allergic disorders<sup>1</sup>;  
Dermatoses<sup>1</sup>; or  
Inflammation<sup>1</sup>, 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.<sup>{R-189}</sup> With acute, short-term conditions, as soon as clinical signs are controlled, the dose should be gradually reduced and then discontinued.<sup>{R-20}</sup> 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:<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-20}</sup>  
0.5 mg (Rx) [*Cortalone*; *Triamtabs*].  
1.5 mg (Rx) [*Cortalone*; *Triamtabs*].

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 0.01 *N* hydrochloric acid in Apparatus 1 at 100 rpm), and Uniformity of dosage units.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

### Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

#### TRIAMCINOLONE ACETONIDE INJECTABLE SUSPENSION USP

##### Usual dose:

Allergic disorders<sup>1</sup>; or  
Dermatoses<sup>1</sup>—*Cats and dogs*: Intramuscular or subcutaneous, 0.11 to 0.22 mg per kg of body weight as a single dose.<sup>{R-22}</sup> If symptoms recur, the dose may be repeated after seven to fifteen days.<sup>{R-22}</sup>  
Note: For dermatitis, 0.22 mg per kg as a single dose is recommended.<sup>{R-22}</sup>

For injections directly into the lesion, a total dose of 1.2 to 1.8 mg as a single dose is used.<sup>{R-22}</sup> 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.<sup>{R-</sup>



Inflammation<sup>1</sup>, including musculoskeletal inflammation—

*Cats and dogs:* Intramuscular or subcutaneous, 0.11 to 0.22 mg per kg of body weight as a single dose.<sup>{R-22}</sup> If symptoms recur, the dose may be repeated after seven to fifteen days.<sup>{R-22}</sup>

*Horses:* Intramuscular or subcutaneous, 0.022 to 0.044 mg per kg of body weight as a single dose.<sup>{R-22}</sup>

Inflammation, musculoskeletal (joint)—

*Cats and dogs:* Intra-articular or intrasynovial, a total dose of 1 to 3 mg as a single dose.<sup>{R-22}</sup> The dose may be repeated after three to four days, if necessary.<sup>{R-22}</sup>

*Horses:* Intra-articular or intrasynovial, 6 to 18 mg as a total single dose.<sup>{R-22}</sup> The dose may be repeated after three to four days, if necessary.<sup>{R-22}</sup>

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.<sup>{R-22}</sup>

[Parturition induction]<sup>1</sup>—Pretreatment dose: *Cattle*—Intramuscular, 0.016 mg per kg of body weight,<sup>{R-110}</sup> 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.<sup>{R-110}</sup>

Note: [Chronic obstructive pulmonary disease]<sup>1</sup>—*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.<sup>{R-199}</sup>

**Strength(s) usually available:**<sup>{R-13}</sup>

U.S.—

Veterinary-labeled product(s):<sup>{R-22}</sup>

2 mg per mL (Rx) [*Vetalog*].

6 mg per mL (Rx) [*Vetalog*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

**Withdrawal times:**

U.S.—Triamcinolone acetonide suspension is not labeled for use in horses intended for food.<sup>{R-22}</sup>

**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.<sup>{R-22}</sup>

**USP requirements:** Preserve in single-dose or in multiple-dose containers, preferably of Type 1 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 endotoxins, and pH (5.0–7.5), and for Injections.<sup>{R-183}</sup>

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

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Developed: 7/15/98

Interim revision: 11/10/99; 2/6/04

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