Rx SOLUTIONS
PEER REVIEWED

PART 1 of a 2-PART SERIES

# Which Drugs Are Most Effective in Managing Atopic Dermatitis?

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## Profile

Canine atopic dermatitis (AD) is a chronic noncurable but manageable inflammatory disease of the skin. Cats also develop allergic skin disease, but its features are generally unique to cats. Medications used to treat allergic skin disease can mask clinical signs but do not change the disease process.

***Multimodal approach*** → Most dermatologists may agree that a multimodal approach can provide the best management of this disease. In dog and cats, the tools used to manage AD focus on[1-3]

- Avoidance of allergens when possible
  —Practically, food and fleas
- Immunotherapy to change the immune response
- Infection control
  —Focus on topical therapy, with use of systemic antimicrobials when necessary
- Skin barrier repair
- Control of itch and inflammation

***Primary treatment options*** → The therapeutic approaches most commonly used for itch and inflammation associated with AD or allergic skin disease in dogs and cats are[1-5]

- Glucocorticoid (antiinflammatory and immunomodulatory) therapy: systemic and topical
- Alternative immunomodulatory strategies (systemic): cyclosporine and oclacitinib

## Glucocorticoid (Antiinflammatory/ Immunomodulatory) Therapy

### Overview

Glucocorticoids have been effective in the management of AD for years,[6] as they have potent effects on many pathways of inflammation and the accompanying itch associated with this disease. Glucocorticoids also have immunomodulatory, antiproliferative, and metabolic effects.

***Multiple modes of action***[6,7] → Genomic effects are mediated by the binding of glucocorticoids to an intracellular glucocorticoid receptor (GR), allowing it to dimerize, become activated, and bind to DNA, where the GR serves as part of a

transcription factor complex to activate or repress gene transcription.

- Ligand-bound GR activates transcription of antiinflammatory genes and represses activation of proinflammatory genes.
- The specific mechanisms of action for glucocorticoids, however, may be cell type and context specific.
  —Much about glucocorticoid function remains unknown.[7]
- The metabolic effects of glucocorticoids include[6,7]
  —Gluconeogenesis in the liver
  —Mobilization of amino acids from extrahepatic sources
  —Inhibition of glucose uptake in muscle and adipose tissue
  —Lipolysis in adipose tissue

***General note*** → 2 distinct glucocorticoid protocols

- Systemic (oral, parenteral)
  —Glucocorticoid therapy may be combined with antihistamine therapy.
- Topical

## Systemic Glucocorticoids: Alone & Combined with Antihistamine

When administered orally for treatment of AD, prednisone, prednisolone, and methylprednisolone are most often selected because their short half-life makes long-term therapy every other day a reasonable choice. These drugs can be used successfully for both short-term itch relief and controlling seasonal allergic disease in dogs and cats. Glucocorticoids can also be used for nonseasonal itch, although it is not uncommon for efficacy to wane.

***Loss of efficacy*** → Has been attributed to tachyphylaxis, the mechanism of which is unknown in dogs and cats

- Although resistance is real, mechanisms are complex. Postulated mechanisms include[8,9]
  —Production of alternative GRs that bind up glucocorticoids but lack antiinflammatory function
  —Reduced levels of *histone deacetylase-2*, an enzyme critical for antiinflammatory function of glucocorticoids

**The specific mechanisms of action for glucocorticoids may be cell type and context specific, although much about their function remains unknown.[7]**

AD = atopic dermatitis,
DNA = deoxyribonucleic acid,
GR = glucocorticoid receptor

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## Glucocorticoid (Antiinflammatory/ Immunomodulatory) Therapy (*continued*)

***Common side effects, all systemic glucocorticoids*** → Include polyuria, polydipsia, and polyphagia, along with behavioral changes[6]

- Long-term effects: hepatic enzyme elevations, catabolism of muscle and fat, potbellied appearance, osteoporosis secondary to decreased calcium uptake and inhibition of bone formation, and delayed wound healing[6]
- Skin effects: thinning of the skin with increased dryness; development of comedones, striae, and milia; and calcinosis cutis[6]
- Increased susceptibility to urinary tract and skin infections has also been noted.[6]
- In cats, diabetes mellitus and development of acquired fragile skin syndrome are concerns.[6]
- **Cautions**
  - —Glucocorticoids are a poor choice for patients with hyperadrenocorticism or diabetes mellitus.
  - —Coadministration of glucocorticoids and NSAIDs is contraindicated.

### Prednisone & Prednisolone

***Formulation*** → Oral (tablet)

***Dose (dogs)*** → 0.5-1 mg/kg PO divided twice a day[10]

- Slow tapering to most effective maintenance dose

***Dose (cats)*** → 1-2 mg/kg PO divided twice a day[10]

- In general, starting doses are double those used in dogs.
  - —Cats may have fewer GRs with lesser affinity for glucocorticoids.[11]
- Although prednisolone is not FDA approved for use in cats, its extralabel use is preferred (see **Key Point**).

**Key Point**

- In cats, use of prednisolone (the active metabolite of prednisone) has been suggested because of poor conversion of prednisone to prednisolone in the liver.
  - —If oral prednisone must be used, consider increasing the dose.

### Methylprednisolone

***Formulation*** → Oral (tablet)

***Dose (dogs, extralabel)*** → Initial induction dose of 0.4-0.5 mg/kg PO once to twice a day[12]

- Slow tapering to most effective maintenance dose

***Dose (cats, extralabel)*** → Initial induction dose of 4 mg/cat PO once a day for cats weighing ≤5 lb and 6 mg/cat for cats weighing >5 lb[12]

- Cats may require higher doses, as they may have fewer GRs in the skin.[11]

**Key Points**

- As compared with prednisone/prednisolone, methylprednisolone may be less likely to cause polyuria and polydipsia.
- Also may be more potent

### Dexamethasone

***Formulation*** → Parenteral (IV, SC), oral (tablet)

***Crisis buster (emergency) dose*** → 0.11-0.22 mg/kg IV (dexamethasone sodium phosphate [SP]) or SC (dexamethasone, dexamethasone SP)[13]

- Dexamethasone 2 mg/mL injectable is FDA approved for use in cats; dexamethasone SP 4 mg/mL is not.

***Oral dose (dogs, extralabel in cats)*** → 0.1-0.3 mg/kg PO once a day[13]

- Taper every 2 to 3 days before stopping.

**Key Points**

- Duration of relief is variable, ranging from 24 to 72 hours, depending on pruritus severity.
- Injections can be used to rapidly reduce pruritus, a method colloquially termed *crisis buster*.
- Oral administration can be used for short-term itch relief.[13]
  - —Especially when patient's itch is refractory to prednisone/prednisolone
  - —Not ideal for long-term use because of its potency and longer duration of action (ie, long biologic activity), which can be problematic regarding adverse effects[6,13]

**Dexamethasone injections can be used to rapidly reduce pruritus, a method commonly referred to as *crisis buster* dosing.**

### Triamcinolone

***Formulation*** → Oral (tablet)

- For topical formulation, see **Topical Glucocorticoids**, page 16.

***Dose (dogs, cats)*** → 0.2-0.4 mg/kg PO once a day[14]

**Key Points**

- Dose designed for short-term itch relief when itch refractory to prednisone/prednisolone
- Not ideal for long-term use because of its potency and longer duration of action (ie, long biologic activity), which can be problematic regarding adverse effects[6]

### Combination Trimeprazine (Antihistamine) & Prednisolone

***Formulation*** → Oral (tablet; trimeprazine 5 mg–prednisolone 2 mg)

***Dose (dogs)*** → Initially, 1 tablet/4.5 kg body weight PO twice a day[15]

FDA = Food and Drug Administration, GR = glucocorticoid receptor, NSAID = nonsteroidal antiinflammatory drug, SP = sodium phosphate

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**Glucocorticoid (Antiinflammatory/ Immunomodulatory) Therapy** *(continued)*

- Taper according to patient needs.
- See **Key Points** for safe steroid dose.
- Owner must administer exactly as directed by veterinarian (based on weight).

***Dose (cats)*** → Not FDA approved for use in cats

- Anecdotal regimen, 1 tablet PO twice a day
  —Taper per patient need.

**Key Points**

- Combination therapy provides relief from itch (trimeprazine) and inflammation (prednisolone).
- **Safe steroid dose**[6]

**Body weight (kg) × 30 = mg dose of steroids per year**
**Example: 10 kg × 30 = 300 mg per year**

  —For combination trimeprazine–prednisolone, this equates to 150 tablets per year or roughly 1 tablet every other day for a 10-kg dog.
- Combination antihistamine–steroid, when used according to the safe steroid dose equation, appears to be associated with minimal risk for serious steroid-associated side effects.[6]
  —Also believed to control itch at lower dose of glucocorticoid than that used with glucocorticoid alone[6]
- Side effects may include drowsiness, excessive thirst and/or urination, dull and dry hair coat, panting, and muscle wasting.[15]

## Topical Glucocorticoids

Topical steroids have been shown to have efficacy for the treatment of canine AD.[16-20] In general, they are most often useful in controlling focal areas of itch, particularly on the fore- and hindfeet. Topical medications containing betamethasone should be restricted to short-term use (10-14 days), as they can induce significant cutaneous adverse effects.[16-20] The low concentrations of triamcinolone in triamcinolone acetonide spray are less likely to have these effects, but use of this agent in small dogs should be monitored.[21] Soft steroid hydrocortisone aceponate may be preferred because although it is potent on the skin, it is metabolized to hydrocortisone by the time it reaches the bloodstream; however, hydrocortisone aceponate is not FDA approved for use in dogs (or cats).[18,19]

***Caution*** → Do not use topical glucocorticoid spray solutions on patients with cutaneous ulcers.

### Triamcinolone Acetonide

***Formulation*** → Topical (spray solution)

- For oral formulation, see **Systemic Glucocorticoids**, page 13.

***Dose (dogs only; US only)*** → Ensure owner compliance with instructions: generally, apply spray twice a day for 7 days, then once a day for 7 days, then every other day or as needed.[21] (Note: Use for longer than 28 days is off-label.)

- Spray areas lightly.
  —Discourage patients from licking areas until the product has dried.
- Safety has not been determined in dogs
  —Weighing <8 lb
  —Younger than 1 year of age

***Dose (cats only)*** → Do not use.

**Key Points**

- Side effects include hives; dyspnea; and swelling of lips, tongue, and face.[21]
  —Skin thinning or fragility, comedones, milia, and calcinosis cutis also can be associated with use of topical triamcinolone.
- Do not use longer than 28 days.[21]

### Hydrocortisone Aceponate

***Formulation*** → Topical (spray solution)

***Dose (dogs, not licensed in United States)***[22] → Ensure owner compliance with instructions: generally, apply 2 pumps per 10 × 10 cm area of skin twice a day for 7 days, then once a day for 7 days, then every other day for additional 14 days.

- Not FDA approved for use in dogs in the United States

***Dose (cats, not licensed in United States)*** → Agent has been shown effective and safe for use in cats when applied at 2 pumps per 10 × 10 cm area of skin once a day for 4 to 6 weeks, then every other day, then twice a week for long-term maintenance.[17]

**Key Points**

- All clinical trials on hydrocortisone aceponate were conducted outside the United States.[22]
- Use for longer than 28 days is off-label.
- No side effects have been reported in dogs treated with hydrocortisone aceponate spray for dermatologic conditions.[22]

**The low concentrations of triamcinolone in triamcinolone acetonide spray are less likely to induce cutaneous adverse effects, but use of this agent in small dogs should be monitored.**[21]

## Alternative Immunomodulatory Strategies (Systemic)

**Key Highlights Featured in Part 2**

Alternative strategies for systemic control of AD include oral cyclosporine in dogs and cats, along with oclacitinib, a new target treatment for canine AD.

***Revolutionized treatment*** → Cyclosporine is a highly recognized alternative treatment for dogs and cats with disease refractory to glucocorticoids.

***Newly targeted drug*** → Learn how oclacitinib specifically targets cytokines involved in the itch and inflammation of AD in dogs.

AD = atopic dermatitis,
FDA = Food and Drug Administration

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## Key Highlights Featured in Part 2 (*continued*)

## Bridging the Gap

Author insights provide guidelines into fine-tuning a multimodal approach to the treatment of AD and allergic skin disease in dogs and cats.

AD = atopic dermatitis

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