APOQUEL® (oclacitinib tablet): Fast-Acting and Safe Itch Relief for Dogs

Your veterinarian has recommended APOQUEL to help control your dog’s itch due to allergic skin disease. APOQUEL provides fast, effective relief from itch and inflammation without many of the side effects associated with steroids.1,2* *Common side effects of steroids include polyuria, polydipsia and polyphagia. Side effects of APOQUEL reported most often are vomiting and diarrhea.

WHAT IS ALLERGIC SKIN DISEASE?

Itching in dogs can be caused by fleas, food or environmental allergens such as pollens, molds or house-dust mites. The 4 most common allergies are:

- **Flea Allergy**
- **Environmental Indoor and Outdoor Allergens** (pollen, dust mites, or mold)
- **Food Allergy**
- **Contact Allergy** (carpet, shampoo, environmental chemicals—pesticides, fertilizers)

WHAT IS APOQUEL USED FOR?

APOQUEL is used for the control of itch associated with allergic skin disease and for control of atopic skin disease in dogs at least 12 months of age. APOQUEL significantly reduces itching, and also decreases the associated inflammation, redness or swelling of the skin.

WHAT CAN I EXPECT WHEN MY DOG RECEIVES APOQUEL?

**Fast Relief**

APOQUEL starts to relieve itch within 4 hours, which is comparable to steroids.3 APOQUEL effectively controls itch within 24 hours.1

**Unique Treatment**

Unlike other treatments, APOQUEL targets a key itch signal in the nervous system and has minimal impact on the immune system. APOQUEL also allows your veterinarian to continue to diagnose the underlying cause of itch while providing your dog with relief.4,4

**Safety**

APOQUEL is safe to use in dogs 12 months of age and older. Additionally, APOQUEL:

- Can be used long-term for maintenance therapy
- Can be used with many other drugs5:
  - Including NSAIDs, anti-infectives, parasiticides, antifungals, and allergen-specific immunotherapy6
  - The use of APOQUEL has not been evaluated in combination with other systemic immunosuppressants, such as corticosteroids and cyclosporine

APOQUEL is not for use in dogs with serious infections, or for use in breeding, pregnant, or lactating dogs.

APOQUEL is not a steroid.

- 55% of dog owners report side effects with steroids5
- Common side effects of steroids include excessive urination, and increased thirst and appetite1,2,6

APOQUEL works differently than steroids.7,8 In a short-term clinical trial, the most common side effects were vomiting and diarrhea similar to those seen with placebo (sugar pills). These side effects occurred in only a small percentage of dogs treated with APOQUEL and typically stopped on their own.1

Weighing the side effects and the need for itch relief can feel like you are on an emotional roller coaster. But, knowing the facts will help you and your dog’s veterinarian make the best choice for relief.

INDICATIONS

Control of pruritus (itching) associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

IMPORTANT SAFETY INFORMATION

Do not use APOQUEL in dogs less than 12 months of age or those with serious infections. APOQUEL may increase the chances of developing serious infections, and may cause existing parasitic skin infestations or pre-existing cancers to get worse. APOQUEL has not been tested in dogs receiving some medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporine. Do not use in breeding, pregnant, or lactating dogs. Most common side effects are vomiting and diarrhea. APOQUEL has been used safely with many common medications including parasiticides, antibiotics and vaccines.

For more information, please see accompanying full Prescribing Information.

Ask your veterinarian about APOQUEL today.
APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety).

**Indications:** Treatment of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

**Dosage and Administration:** The dose of APOQUEL (oclacitinib tablet) tablets is 0.18 to 0.27 mg oclacitinib/lb (0.4 to 0.6 mg oclacitinib/kg) body weight, administered orally, twice daily for 14 days, and then administered once daily for maintenance therapy. APOQUEL may be administered with or without food.

**Dosing Chart**

<table>
<thead>
<tr>
<th>Weight Range (in lb)</th>
<th>Number of Tablets to be Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>6.6</td>
<td>9.9</td>
</tr>
<tr>
<td>10.0</td>
<td>14.4</td>
</tr>
<tr>
<td>15.0</td>
<td>19.9</td>
</tr>
<tr>
<td>20.0</td>
<td>26.9</td>
</tr>
<tr>
<td>30.0</td>
<td>44.9</td>
</tr>
<tr>
<td>45.0</td>
<td>59.9</td>
</tr>
<tr>
<td>60.0</td>
<td>89.9</td>
</tr>
<tr>
<td>90.0</td>
<td>129.9</td>
</tr>
<tr>
<td>130.0</td>
<td>175.9</td>
</tr>
</tbody>
</table>

**Warnings:**

- APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety).
- APOQUEL may increase susceptibility to infection, including demodicosis, and exacerbate neoplastic conditions (see Adverse Reactions and Animal Safety).

**Human Warnings:**

This product is not for human use. Keep this and all drugs out of reach of children. For use in dogs only. Wash hands immediately after handling the tablets. In case of accidental eye contact, flush immediately with water or saline for at least 15 minutes and then seek medical attention. In case of accidental ingestion, seek medical attention immediately.

**Precautions:**

- APOQUEL is not for use in breeding dogs, or pregnant or lactating bitches.
- The use of APOQUEL has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents.
- Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.

**Adverse Reactions:**

- Control of Atopic Dermatitis

In masked field studies, APOQUEL was compared to placebo in dogs with atopic dermatitis. Dogs were treated with tablets at the labeled dose of 0.4 mg/kg for 28 days. APOQUEL was well tolerated, with a favorable safety profile. The most commonly reported adverse events were diarrhea, vomiting, and lethargy. Neoplasms were reported in 3% of dogs treated with placebo and 3% of dogs treated with APOQUEL. One dog developed a malignant melanoma after 112 days of APOQUEL administration.

**Continuation Field Study**

A continuation field study after completion of the initial masked field study was conducted to assess the long-term safety and efficacy of APOQUEL. Dogs were randomized to receive placebo or APOQUEL at the labeled dose. Neoplasms were reported in 3% of dogs treated with placebo and 3% of dogs treated with APOQUEL. One dog developed a malignant melanoma after 112 days of APOQUEL administration.

**Pharmacokinetics:**

Oclacitinib is rapidly absorbed following oral administration, with peak plasma concentrations (Cmax) of less than 1 hour. The absolute bioavailability of oclacitinib is 89%.

**Mechanism of Action**

Oclacitinib inhibits the function of a variety of pruritogenic cytokines and pro-inflammatory cytokines, as well as cytokines involved in hematopoiesis that are dependent on JAK2. Oclacitinib is not a corticosteroid or antihistamine.

**Clinical Pharmacology**

- Pharmacokinetics

In dogs, oclacitinib maleate is rapidly and well absorbed following oral administration, with mean time to peak plasma concentrations (tmax) of 1.7 hours. The absolute bioavailability of oclacitinib is 89%.

- Pharmacodynamics

Oclacitinib is metabolized in the liver and excreted mainly in the bile. The elimination half-life of oclacitinib is approximately 12 hours. The major metabolic pathways of oclacitinib are glucuronidation and sulfonation.

**For oral use in dogs only**

Caution: Federal (USA) Law restricts this drug to use by or on the order of a licensed veterinarian.

**Description:** APOQUEL (oclacitinib maleate) is a synthetic Janus Kinase (JAK) inhibitor. The chemical composition of APOQUEL is N-methyl-[trans-4-(methyl-7H-pyrrolo[2,3-d]pyrimidin-4-ylamino)cyclohexyl]methanesulfonamide (2Z)-2-butenedioate.

**Composition:** The chemical structure of oclacitinib maleate is:

![Chemical Structure of Oclacitinib Maleate](image)

**Mechanism of Action:**

Oclacitinib inhibits the function of a variety of pruritogenic cytokines and pro-inflammatory cytokines, as well as cytokines involved in hematopoiesis that are dependent on JAK2. Oclacitinib is not a corticosteroid or antihistamine.

**For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at [http://www.fda.gov/AnimalVeterinary/SafetyHealth](http://www.fda.gov/AnimalVeterinary/SafetyHealth).**
Effectiveness:  
Control of Atopic Dermatitis  
A double-masked, 112-day, controlled study was conducted at 18 U.S. veterinary hospitals. The study enrolled 299 client-owned dogs with atopic dermatitis. Dogs were randomized to treatment with APOQUEL (152 dogs: tablets administered at a dose of 0.4-0.6 mg/kg per dose twice daily for 14 days and then once daily) or placebo (147 dogs: vehicle control, tablets administered on the same schedule). During the study, dogs could not be treated with other drugs that could affect the assessment of effectiveness, such as corticosteroids, anti-histamines, or cyclosporine. Treatment success for pruritus for each dog was defined as at least a 2 cm decrease from baseline on a 10 cm visual analog scale (VAS) in pruritus, assessed by the Owner, on Day 28. Treatment success for skin lesions was defined as a 50% decrease from the baseline Canine Atopic Dermatitis Extent and Severity Index (CADESI) score, assessed by the Veterinarian, on Day 28. The estimated proportion of dogs with Treatment Success in Owner-assessed pruritus VAS score and in Veterinarian-assessed CADESI score was greater and significantly different for the APOQUEL group compared to the placebo group.

Estimated Proportion of Dogs with Treatment Success, Atopic Dermatitis

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>APOQUEL (n = 134)</th>
<th>Placebo (n = 203)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owner-Assessed Pruritus VAS</td>
<td>0.66 (n = 134)</td>
<td>0.04 (n = 133)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Veterinarian-Assessed CADESI</td>
<td>0.49 (n = 134)</td>
<td>0.04 (n = 134)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Compared to the placebo group, mean Owner-assessed pruritus VAS scores (on Days 1, 2, 7, 14, and 28) and Veterinarian-assessed CADESI scores (on Days 14 and 28) were lower (improved) in dogs in the APOQUEL group. By Day 30, 86.4% (127/147) of the placebo group dogs and 15% (23/150) of the APOQUEL group dogs withdrew from the masked study because of worsening clinical signs, and had the option to enroll in an unmasked study and receive APOQUEL. For dogs that continued APOQUEL treatment beyond one month, the mean Owner-assessed pruritus VAS scores and Veterinarian-assessed CADESI scores continued to improve through study end at Day 112.

Control of Pruritus Associated with Allergic Dermatitiss

A double-masked, 30-day, controlled study was conducted at 26 U.S. veterinary hospitals. The study enrolled 436 client-owned dogs with a history of allergic dermatitis attributed to one or more of the following conditions: atop dermatitis, flea allergy, food allergy, contact allergy, and other/unspecified allergic dermatitis. Dogs were randomized to treatment with APOQUEL (216 dogs: tablets administered at a dose of 0.4-0.6 mg/kg twice daily) or placebo (220 dogs: vehicle control, tablets administered twice daily). During the study, dogs could not be treated with other drugs that could affect the assessment of pruritus or dermal inflammation such as corticosteroids, anti-histamines, or cyclosporine. Treatment success for each dog was defined as at least a 2 cm decrease from baseline on a 10 cm visual analog scale (VAS) in pruritus, assessed by the Owner, on at least 5 of the 7 evaluation days. The estimated proportion of dogs with Treatment Success was greater and significantly different for the APOQUEL group compared to the placebo group.

Owner-Assessed Pruritus VAS Treatment Success, Allergic Dermatitis

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>APOQUEL (n = 203)</th>
<th>Placebo (n = 204)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated Proportion of Dogs with Treatment Success</td>
<td>0.67</td>
<td>0.29</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

After one week of treatment, 86.4% of APOQUEL group dogs compared with 42.5% of placebo group dogs had achieved a 2 cm reduction on the 10 cm Owner-assessed pruritus VAS. On each of the 7 days, mean Owner-assessed pruritus VAS scores were lower in dogs in the APOQUEL group (See Figure 1). Veterinarians used a 10 cm VAS scale to assess each dog’s dermatitis. After one week of treatment, the mean Veterinarian-assessed VAS dermatitis score for the dogs in the APOQUEL group was lower at 2.2 cm (improved from a baseline value of 6.2 cm) compared with the placebo group mean score of 4.9 cm (from a baseline value of 6.2 cm). For dogs that continued APOQUEL treatment beyond one week, the Veterinarian-assessed dermatitis scores continued to improve through study end at Day 30.

Figure 1: Owner Assessed Pruritus VAS Scores by treatment for Days 0-7

Animal Safety:

Margin of Safety in 12 Month Old Dogs
Oclacitinib maleate was administered to healthy, one-year-old Beagle dogs twice daily for 6 weeks, followed by once daily for 20 weeks, at 0.6 mg/kg (1X maximum exposure dose, 8 dogs), 1.8 mg/kg (3X, 8 dogs), and 3.0 mg/kg (5X, 8 dogs) oclacitinib for 28 weeks. Eight dogs received placebo (empty gelatin capsule) at the same dosage schedule. Clinical observations that were considered likely to be related to oclacitinib maleate included papillomas and a dose-dependent increase in the number and frequency of interdigital furunculosis (cysts) on one or more feet during the study. Additional clinical observations were primarily related to the interdigital furunculosis and included dermatitis (alopecia, erythema, abrasions, scabbing/crusts, and edema of feet) and lymphadenopathy of peripheral nodes. Microscopic findings considered to be oclacitinib maleate-related included decreased cellularity (lymphoid) in Gut-Associated Lymphoid Tissue (GALT), spleen, thymus, cervical and mesenteric lymph node; and decreased cellularity of sternal and femoral bone marrow. Lymphoid hyperplasia and chronic active inflammation was seen in lymph nodes draining feet affected with interdigital furunculosis. Five oclacitinib maleate-treated dogs had microscopic evidence of mild interstitial pneumonia. Clinical pathology findings considered to be oclacitinib maleate-related included mild, dose-dependent reduction in hemoglobin, hematocrit, and reticulocyte counts during the twice daily dosing period with decreases in the leukocyte subsets of lymphocytes, eosinophils, and basophils. Total proteins were decreased over time primarily due to the albumin fraction.

Vaccine Response Study
An adequate immune response (serology) to killed rabies (RV), modified live canine distemper virus (CDV), and modified live canine parvovirus (CPV) vaccination was achieved in eight 16-week old vaccine naïve puppies that were administered oclacitinib maleate at 1.8 mg/kg oclacitinib (3X maximum exposure dose) twice daily for 84 days. For modified live canine parvovirus vaccine (CPV), > 80% (6 of 8) of the dogs achieved adequate serologic response. Clinical observations that were considered likely to be related to oclacitinib maleate treatment included enlarged lymph nodes, interdigital furunculosis, cysts, and pododermatitis. One oclacitinib maleate-treated dog (26-weeks-old) was euthanized on Day 74 after physical examination revealed the dog to be febrile, lethargic, with pale mucous membranes and frank blood in stool. Necropsy revealed lesions consistent with sepsis secondary to immunosuppression. Bone marrow hyperplasia was consistent with response to sepsis.

Marginal Safety in 6 Month Old Dogs
A margin of safety in 6-month-old dogs was discontinued after four months due to the development of bacterial pneumonia and generalized demodec mange infections in dogs in the high dose (3X and 5X) treatment groups, dosed at 1.8 and 3.0 mg/kg oclacitinib twice daily, for the entire study.

Storage Conditions:
APOQUEL should be stored at controlled room temperature between 20° to 25°C (68° to 77°F) with excursions between 15° to 40°C (59° to 104°F).

How Supplied:
APOQUEL tablets contain 3.6 mg, 5.4 mg, or 16 mg of oclacitinib as oclacitinib maleate per tablet. Each strength tablets are packaged in 20 and 100 count bottles. Each tablet is scored and marked with AQ and either an S, M, or L that correspond to the different tablet strengths on both sides.

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Made in Italy

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