APOQUEL® (oclacitinib tablet): Fast-Acting and Safe Itch Relief So Your Dog and You Can Return to Normal

Your veterinarian has recommended APOQUEL to help control your dog's itch due to allergic skin disease. APOQUEL provides fast, long-term relief from itch and inflammation without many of the side effects associated with some other treatments.1-3

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 (such as pollen, dust mites, or mold)
- FOOD ALLERGY
- CONTACT ALLERGY (carpet, deodorant, shampoo, insecticidal products)

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 1 year 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 the itch within 4 hours, comparable to steroids.3
- APOQUEL effectively controls the itch within 24 hours.1
- APOQUEL relieves itch in the long term.3

Unique Treatment

- Unlike other treatments, APOQUEL targets a key itch signal in the nervous system and has minimal negative 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.3,4

Short- and Long-Term Safety

- Without many of the side effects associated with some other treatments.1,2

APOQUEL: FAST and SAFE itch relief that helps restore the quality of life for your dog and for you.

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 cyclosporines. 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.


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Dogs that withdrew from the masked field study could enter an unmasked study where all dogs received APOQUEL. Between the masked and unmasked study, 239 dogs received at least one dose of APOQUEL. Of these 239 dogs, two dogs were withdrawn from study due to suspected treatment-related adverse reactions: one dog had an intense flare-up of dermatitis and secondary pyoderma after 19 days of APOQUEL treatment, and another dog developed generalized pruritus after 25 days of APOQUEL administration. Two other dogs on APOQUEL were withdrawn from study due to suspected or confirmed malignant neoplasia and subsequently euthanized, including one dog that developed a Grade III mast cell tumor after 60 days of APOQUEL administration. Of the 147 dogs in the placebo group developed a Grade I mast cell tumor and was withdrawn from the masked study. Additional dogs receiving APOQUEL were hospitalized for diagnosis and treatment of pneumonia (one dog), transient bloody vomiting and stool (one dog), and cystitis with urinalysis (one dog).

In the 283 dogs that received APOQUEL, the following adverse events were reported: diarrhea (10.8%), vomiting (8.9%), and lethargy (1 dog). Dogs in the APOQUEL group had a slight decrease in mean white blood cell counts (neutrophil, eosinophil, and monocyte counts) that remained within the normal reference range. Mean lymphocyte count for dogs in the APOQUEL group increased at Day 7, but returned to pretreatment levels by study end without a break in APOQUEL administration. Serum cholesterol increased in 25% of APOQUEL group dogs, but mean cholesterol remained within the reference range.

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

The chemical structure of oclacinib maleate is:

![Chemical Structure Image]

**Table: Dosing Chart**

<table>
<thead>
<tr>
<th>Weight Range (in lb)</th>
<th>Weight Range (in Kg)</th>
<th>Number of Tablets to be Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.6</td>
<td>3.0</td>
<td>3.6 mg Tablets</td>
</tr>
<tr>
<td>10.0</td>
<td>4.5</td>
<td>5.4 mg Tablets</td>
</tr>
<tr>
<td>15.0</td>
<td>6.9</td>
<td>16 mg Tablets</td>
</tr>
<tr>
<td>20.0</td>
<td>9.0</td>
<td>0.5</td>
</tr>
<tr>
<td>30.0</td>
<td>13.6</td>
<td>0.5</td>
</tr>
<tr>
<td>45.0</td>
<td>20.9</td>
<td>0.5</td>
</tr>
<tr>
<td>60.0</td>
<td>27.0</td>
<td>0.5</td>
</tr>
<tr>
<td>90.0</td>
<td>40.0</td>
<td>16 mg Tablets</td>
</tr>
<tr>
<td>130.0</td>
<td>55.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**Warnings:**

APOQUEL is not for use in dogs with sensitivity to oclacinib maleate, including dogs with known or suspected dermatologic conditions. APOQUEL may increase susceptibility to infections, including diarreahoea, 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 immediately.

**Precautions:**

APOQUEL is not for use in breeding dogs, pregnant or lactating bitches. The use of APOQUEL has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents.

**Adverse Reactions:**

Control of Atopic Dermatitis

In a masked field study to assess the efficacy and safety of oclacinib for the control of atopic dermatitis in dogs, 152 dogs treated with APOQUEL and 147 dogs treated with placebo (vehicle control) were evaluated for safety. The majority of dogs in the placebo group withdrew from the 112-day study by Day 16. Adverse reactions reported and their incidence are detailed below. Dogs on APOQUEL had decreased leukocytes (neutrophil, eosinophil, and monocyte counts) and increased cholesterol and lipase compared to the placebo group but group means remained within the normal range. Mean lymphocyte counts were transiently increased at Day 14 in the APOQUEL group.

- Mean lymphocyte count for dogs in the APOQUEL group increased at Day 7, but returned to pretreatment levels by study end without a break in APOQUEL administration. Serum cholesterol increased in 25% of APOQUEL group dogs, but mean cholesterol remained within the reference range.

Control of Pruritus Associated with Allergic Dermatities

In a masked field study to assess the effectiveness and safety of oclacinib for the control of pruritus associated with allergic dermatitis in dogs, 216 dogs treated with APOQUEL and 270 dogs treated with placebo (vehicle control) were evaluated for safety. During the 30-day study, there were no fatalities and no adverse reactions resulting in hospital care. Adverse reactions reported and their incidence are detailed below. Dogs on APOQUEL had decreased leukocytes (neutrophil, eosinophil, and monocyte counts) and increased cholesterol and lipase compared to the placebo group but group means remained within the reference range. In dogs on APOQUEL treated with oclacinib for pruritus, tumors and/or neoplasms were identified in all tissues. Dogs on oclacinib had an increased frequency of tumors and/or neoplasms compared to the placebo group (see Adverse Reactions and Animal Safety).
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 confirmed 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 = 203)</th>
<th>Placebo (n = 204)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owner-Assessed Pruritus VAS</td>
<td>0.67</td>
<td>0.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Veterinarian-Assessed CADESI</td>
<td>0.49</td>
<td>0.04</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 Veteraninarian-assessed CADESI scores (on Days 14 and 28) were lower (improved) in dogs in the APOQUEL group. By Day 30, 90% (227/244) of the placebo group dogs and 11% (25/220) 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 Atopic Dermatitis
A double-masked, 50-day, controlled study was conducted at 26 U.S. veterinary hospitals. The study enrolled 496 client-owned dogs with a history of allergic dermatitis attributed to one or more of the following conditions: atopic dermatitis, flea allergy, food allergy, contact allergy, and other unclassified 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 (280 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 dermatological 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, Atopic Dermatitis

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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.

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 (5X maximum exposure dose, 8 dogs), 1.6 mg/kg (5X, 8 dogs), and 3.0 mg/kg (5X, 8 dogs) oclacitinib for 26 weeks. Eight dogs received placebo (empty gelatin capsule) at the same dosing 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 (local alopecia, erythema, abrasions, scabbing/crusts, and edema) of feet and lymphangiopathy of peripheral microcots. Microscopic findings considered to be oclacitinib maleate-related included decreased colliquatory lymphocytes in Gut-Associated Lymphoid Tissue (GALT), spleen, thymus, and mesenteric lymph nodes, 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 protein were decreased over time primarily due to the albumin fraction.

Vaccine Response Study
An adequate immune response (serology) to killed rabies (R), modified live canine parvovirus (CPV, < 80% (6 of 8) of the dogs achieved adequate serology 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 (28-week-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 hypoplasia was consistent with response to sepsis.

Margin of Safety in 6 Month Old Dogs
A margin of safety study in 6-month-old dogs was discontinued after four months due to the development of bacterial pneumonia and generalized demodex mange infections in the high dose (5X and 5X) treatment groups, dosed at 1.0 and 1.5 mg/kg oclacitinib twice daily, for the entire study.

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

How Supplied:
APOQUEL tablets contain 0.6 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 APOQUEL 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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