Set expectations and collaborate with pet owners to treat flares

Allergic dermatitis can require lifelong management—even when controlled, occasional flares can happen. Pet owners may lose confidence in their dog’s allergic treatment if a flare occurs.

Consider relying on the 80/80 rule—a goal of relieving 80% of their dog’s itch 80% of the time.

- Schedule an exam to evaluate the flare
- Identify the cause
- Stay the course with anchor therapy
- Provide individualized therapy as needed

Can be used as needed to relieve pruritus during a flare of allergic dermatitis
When there is a flare of pruritus: identify the cause with the diagnostic approach

Complete a diagnostic workup and identify the underlying cause

With flares, be aware of:¹

• Fleas
• Skin and ear infections caused by bacteria and yeast
• Food allergy
• House dust mites, pollen and mold

Stop the pruritus

Rule out parasites

Treat skin infection

Conduct food trial

Confirm atopic dermatitis

Can be used:

• To relieve allergic pruritus during a diagnostic workup
• To treat flares of allergic dermatitis

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

Apoquel 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. Consider the risks and benefits of treatment in dogs with a history of recurrence of these conditions. New neoplastic conditions (benign and malignant) were observed in clinical studies and post-approval. 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 full Prescribing Information.

Cytopoint Indications: Cytopoint has been shown to be effective for the treatment of dogs against allergic dermatitis and atopic dermatitis.
Immunomodulator

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-7-hydroxy-2,3-dipryrimidin-4-ylamino) cyclohexyl)methanesulfonamide (2Z)-2-butenedioate.

The chemical structure of oclacitinib maleate is:

![Chemical Structure of Oclacitinib Maleate]

**Indications:** Control 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 maleate) tablets is 0.18 to 0.27 mg oclacitinib/b (0.4 to 0.6 mg oclacitinib/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.

**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>Low</td>
<td>High</td>
<td>3.6 mg Tablets</td>
</tr>
<tr>
<td>6.6</td>
<td>9.9</td>
<td>3.0</td>
</tr>
<tr>
<td>10.0</td>
<td>14.9</td>
<td>4.5</td>
</tr>
<tr>
<td>15.0</td>
<td>19.9</td>
<td>6.0</td>
</tr>
<tr>
<td>20.0</td>
<td>29.9</td>
<td>9.0</td>
</tr>
<tr>
<td>30.0</td>
<td>44.9</td>
<td>13.5</td>
</tr>
<tr>
<td>45.0</td>
<td>59.9</td>
<td>20.0</td>
</tr>
<tr>
<td>60.0</td>
<td>89.9</td>
<td>27.0</td>
</tr>
<tr>
<td>90.0</td>
<td>129.9</td>
<td>40.0</td>
</tr>
<tr>
<td>130.0</td>
<td>175.9</td>
<td>55.0</td>
</tr>
</tbody>
</table>

**Warnings:**
- APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety).
- APOQUEL modulates the immune system.
- APOQUEL is not for use in dogs with serious infections.
- APOQUEL may increase susceptibility to infection, including demodicosis, and exacerbation of neoplastic conditions (see Precautions, Adverse Reactions, Post-Approval Experience, and Animal Safety).

New neoplastic conditions (benign and malignant) were observed in dogs treated with APOQUEL during clinical studies and have been reported in the post-approval period (see Adverse Reactions and Post-Approval Experience).

Consider the risks and benefits of treatment prior to initiating APOQUEL in dogs with a history of recurrent serious infections or recurrent demodicosis or neoplasia (see Adverse Reactions, Post-Approval Experience, 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: Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.
- The use of APOQUEL has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents. APOQUEL is not for use in breeding dogs, or pregnant or lactating bitches.

**Adverse Reactions:**

**Control of Atopic Dermatitis:**

In a masked field study to assess the effectiveness and safety of oclacitinib 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 percent of dogs affected) during Days 0-16 included diarrhea (4.6% APOQUEL, 3.4% placebo), vomiting (3.9% APOQUEL, 4.1% placebo), anorexia (2.6% APOQUEL, 0% placebo), new cutaneous or subcutaneous lumps (2.6% APOQUEL, 2.7% placebo), and lethargy (1.8% APOQUEL, 3.4% placebo). In most cases, diarrhea, vomiting, anorexia, and lethargy spontaneously resolved with continued dosing. Dogs on APOQUEL had decreased leukocytes (neutrophil, eosinophil, and monocyte counts) and serum globulin, 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.

Dogs that withdrew from the masked field study could enter an unmasked study where all dogs received APOQUEL. Between the masked and unmasked study, 283 dogs received at least one dose of APOQUEL. Of these 283 dogs, two were withdrawn from study due to suspected treatment-related adverse reactions: one dog that had an intense flare-up of dermatitis and severe secondary pyoderma after 19 days of APOQUEL administration, and one dog that developed generalized demodicosis after 28 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 signs associated with a heart base mass after 21 days of APOQUEL administration, and one dog that developed a Grade III mast cell tumor after 60 days of APOQUEL administration.

One 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 urolithiasis (one dog).

In the 283 dogs that received APOQUEL, the following additional clinical signs were reported after beginning APOQUEL (percentage of dogs with at least one report of the clinical sign as a non-pre-existing finding): pyoderma (12.0%), non-specific dermal lumps (12.0%), otitis (9.9%), vomiting (9.2%), diarrhea (8.0%), histiocytoma (3.9%), cystitis (3.5%), anorexia (3.2%), lethargy (2.8%), yeast skin infections (2.5%), pododermatitis (2.5%), lipoa (2.1%), polydipsia (1.4%), lymphadenopathy (1.1%), nausea (1.1%), increased appetite (1.1%), aggression (1.1%), and weight loss (0.7%).

**Control of Pruritus Associated with Allergic Dermatitis:**

In a masked field study to assess the effectiveness and safety of oclacitinib for the control of pruritus associated with allergic dermatitis in dogs, 216 dogs treated with APOQUEL and 220 dogs treated with placebo (vehicle control) were evaluated for safety. During the 30-day study, there were no fatalities and no adverse reactions requiring hospital care. Adverse reactions reported (and percent of dogs affected) during Days 0-7 included diarrhea (2.3% APOQUEL, 0.9% placebo), vomiting (2.3% APOQUEL, 1.8% placebo), lethargy (1.8% APOQUEL, 1.4% placebo), anorexia (1.4% APOQUEL, 0% placebo), and polydipsia (1.4% APOQUEL, 0% placebo). In most of these cases, signs spontaneously resolved with continued dosing. Five APOQUEL group dogs were withdrawn from study because of: darkening areas of skin and fur (1 dog); diarrhea (1 dog); fever, lethargy and cystitis (1 dog); an inflamed footpad and vomiting (1 dog); 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.

**Continuation Field Study**

After completing APOQUEL field studies, 239 dogs enrolled in an unmasked (no placebo control) continuation therapy study receiving APOQUEL for an unrestricted period of time. Mean time on study was 372 days (range 1 to 610 days). Of the dogs enrolled, one dog developed demodicosis following 273 days of APOQUEL administration. One dog developed dermal pigmented viral plaques following 266 days of APOQUEL administration. One dog developed a moderately severe bronchopneumonia after 272 days of APOQUEL administration; this infection resolved with antimicrobial treatment and temporary discontinuation of APOQUEL. One dog was euthanized after developing abdominal ascites and pleural effusion of unknown etiology after 450 days of APOQUEL administration. Six dogs were euthanized because of suspected malignant neoplasms: including thoracic metastatic, abdominal metastatic, splenic, frontal sinus, and intracranial neoplasms, and transitional cell carcinoma after 17, 120, 175, 49, 141, and 286 days of APOQUEL administration, respectively. Two dogs each developed a Grade II mast cell tumor after 52 and 91 days of APOQUEL administration, respectively. One dog developed low grade B-cell lymphoma after 392 days of APOQUEL administration. Two dogs each developed an apparent grade IV adenocarcinoma (one dermal, one anal sac) after approximately 210 and 320 days of APOQUEL administration, respectively. One dog developed a low grade oral spindle cell sarcoma after 320 days of APOQUEL administration.

**Post-Approval Experience (2020):**

The following adverse events are based on post-approval drug experience data for APOQUEL. Not all adverse events are reported to FDA/CFVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported in dogs are listed in decreasing order of reporting frequency.

- Vomiting, lethargy, anorexia, diarrhea, elevated liver enzymes, dematitiss (i.e. crusts, pododermatitis, pyoderma), seizures, polydipsia, and demodicosis.
- Benign, malignant, and unclassified neoplasms, dermal masses (including papillomas and histiocytomas), lymphoma and other cancers have been reported.
- Death (including euthanasia) has been reported.

**Contact Information:**
- To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet, contact Zoetis Inc. at 1-888-963-8471 or www.zoetis.com.
- For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.
Oclacitinib inhibits the function of a variety of pruritogenic cytokines and pro-inflammatory cytokines, as well as cytokines involved in allergic dermatitis that are dependent on JAK1 or JAK3 enzyme activity. It has little effect on cytokines involved in hematopoiesis that are dependent on JAK2.

Mechanism of Action

Oclacitinib is metabolized in the dog to multiple metabolites and one major oxidative metabolite was identified in plasma and urine. Overall the major clearance route is metabolism with minor contributions from renal and biliary elimination. Inhibition of canine cytokine P450 enzymes by oclacitinib is minimal; the inhibitory concentrations (IC50s) are 50 fold greater than the observed Cmax, values used in use doses.

Mean (95% CL) total body oclacitinib clearance from plasma was ~316 (237, 398) mL/h/kg body weight (5.3 mL/min/kg body weight). Following IV and PO administration, the terminal t1/2 appeared similar with mean values of 3.5 (2.2, 4.7) and 4.1 (3.1, 5.2) hours, respectively.

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 score on a 10 cm VAS in 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.

Effectiveness Parameter | APOQUEL | Placebo | P-value
--- | --- | --- | ---
Owner-Assessed Pruritus VAS | 0.66 (n = 131) | 0.04 (n = 133) | <0.0001
Veterinarian-Assessed CADESI | 0.49 (n = 134) | 0.04 (n = 134) | <0.0001

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% (127/147) of the placebo group dogs and 15% (37/245) of the APOQUEL group dogs were completely clear of skin lesions. Treatment success for pruritus by Day 28 was similar to that observed by Day 30. The estimated proportion of dogs with Treatment Success was greater and significantly different for the APOQUEL group compared to the placebo group.

Estimated Proportion of Dogs with Treatment Success, Atopic Dermatitis

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). At the end of the study, 216 dogs were randomized to treatment with APOQUEL (152 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 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 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.

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>APOQUEL</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owner-Assessed Pruritus VAS</td>
<td>0.67 (n = 203)</td>
<td>0.29 (n = 204)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Approved by FDA under NADA # 141-345