A fAst-Acting And sAfe treAtment thAt you cAn turn to first for the control of itching in dogs cAused by Allergic skin diseAse...

APOQUEL is a novel treatment that provides fast and safe relief from itching and inflammation, without many of the side effects seen with other medications.1,2

APOQUEL® (oclacitinib tablet)

A HELPFUL GUidE tO tALkinG tO YOUr CLiENTs AbOUt CAninE ALLErGiC skin disEAsE And APOQUEL.

This tool is for educational purposes only. Please use this tool with pet owners so they know what to expect from treatment with APOQUEL. Please see full Prescribing Information for APOQUEL inside pocket.

## WHY APOQUEL AND NOT STEROIDS?

Previously, the only available treatment that would provide dogs with rapid relief from itching was steroids. But steroids come with potential side effects in the short term, such as:

- Panting5
- More frequent urination5

Steroids are not recommended for long-term use because they can cause even more harmful side effects. Now there is APOQUEL, a targeted therapy that:

- Is FDA-approved
- Works as fast as steroids in controlling allergic skin disease without many of the side effects seen with steroid use1,2
- Is proven safe to use long term6

## HOW IS APOQUEL DOSED?

APOQUEL should be given twice daily up to 14 days of therapy and once daily thereafter for maintenance.

- APOQUEL may be given with or without food
- APOQUEL may be used with many other common therapies

<table>
<thead>
<tr>
<th>THERAPY</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-steroidal anti-inflammatory drugs (NSAIDs)</td>
<td>Carprofen</td>
</tr>
<tr>
<td>Vaccines</td>
<td>Vanguard High Titer6</td>
</tr>
<tr>
<td>Allergy shots</td>
<td>Allergen-specific immunotherapy</td>
</tr>
</tbody>
</table>

**Indication**
Control of pruritus (itch) 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 infections 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. Please see full Prescribing Information for APOQUEL inside pocket.

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**REFERENCES**

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WHAT IS ALLERGIC SKIN DISEASE?

There are 4 common allergic skin diseases of the dog:

• flea allergy
• food allergy
• contact allergy
• atopic dermatitis (a chronic itchy skin disease associated with environmental allergens)

Our clinic recommends APOQUEL® (oclacitinib tablet) to control your dog’s itch and inflammation associated with allergic skin disease.

WHAT IS APOQUEL?

APOQUEL® is a prescription medication used for the control of itching associated with allergic skin disease and for the control of atopic dermatitis in dogs at least 12 months of age. APOQUEL lessens dog itch and the desire to scratch and also decreases the inflammation or swelling of the skin.1,2

APOQUEL is not a steroid, cyclosporine or antihistamine. It is a new class of drug that has fewer side effects than you may have seen with other therapies.2

WHAT CAN I EXPECT FROM MY DOG’S TREATMENT WITH APOQUEL?

With APOQUEL your dog will begin to heal quickly

• Starts to relieve the itch within 4 hours. Effectively controls itch within 24 hours1,4
• You should see a reduction in the redness and irritation of your dog’s skin1,5
• Side effects of APOQUEL were similar to placebo without many of the side effects associated with the use of steroids (such as excessive panting, hunger, urination, and Cushing’s Disease).1,5
  - The most common side effects of APOQUEL were vomiting and diarrhea. These side effects usually stopped on their own.
A fast-acting and safe treatment that you can turn to first for the control of itching in dogs caused by allergic skin disease...

APOQUEL is a novel treatment that provides fast and safe relief from itching and inflammation, without many of the side effects seen with other medications.1,2

**APOQUEL® (oclacitinib tablet)**

**A helpful guide to talking to your clients about canine allergic skin disease and APOQUEL.**

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**THERAPY**

- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Vaccines
- Allergy shots

**EXAMPLES**

- Carprofen
- Vanguard High Titer®
- Allergen-specific immunotherapy

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Please see full Prescribing Information for APOQUEL inside pocket.

**UNIQUE**

APOQUEL® is the only treatment specifically designed to go straight to the source of the dog’s itch with minimal negative impact on the rest of a dog’s body3

**FAST**

Starts to relieve the dog’s itch within 4 hours. Effectively controls itch within 24 hours1,4

**SAFE**

Relief without many of the side effects associated with other treatments1,2

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Relief without many of the side effects associated with other treatments1,2

...that helps restore the quality of life for the dog and for you.

THERAPY

Non-steroidal anti-inflammatory drugs (NSAIDs)

Vaccines

Allergy shots

EXAMPLES

Carprofen

Vanguard High Titer8

Allergen-specific immunotherapy

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Please see full Prescribing Information for APOQUEL inside pocket.
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-methyltrans-4-(methyl-7H-pyrrolo[2,3-d]pyrimidin-4-ylamino)cyclohexyl methanesulfonamide (2Z)-2-butenamide.

The chemical structure of oclacitinib maleate is:

![Chemical Structure of Oclacitinib Maleate](image)

Weight Range
14.9 - 19.9
54.9
8.9
3.6
mg
-0.5
80.0
13.4
Low
-18
Dosing Chart
once daily for maintenance therapy. APOQUEL may be administered with or without food.

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

Dose and Administration: The dose of APOQUEL (oclacitinib maleate) 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 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>14.5</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>44.3</td>
<td>13.5</td>
</tr>
<tr>
<td>45.0</td>
<td>59.9</td>
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</tr>
<tr>
<td>60.0</td>
<td>89.0</td>
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<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 is not for use in dogs with serious infections. 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.

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.

Reactions: Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.

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 (4.8% APOQUEL, 3.4% placebo), vomiting (3.9% APOQUEL, 4.1% placebo), anorexia (2.6% APOQUEL, 0% placebo), decreased normal lymphocyte counts, decreased neutrophil counts, decreased monocyte counts, and decreased total 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 this study was 372 days (range 1 to 610 days). Of these 239 dogs, 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 developed an apocrine gland adenocarcinoma (one dermal, one anal sac) after approximately 120 and 300 days of APOQUEL administration, respectively. One dog developed a low grade oral spindle cell sarcoma after 320 days of APOQUEL administration.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, 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 http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology: Mechanism of Action

Oclacitinib inhibits the function of a variety of pruritogenic cytokines and pro-inflammatory cytokines, as well as cytokines involved in allergy that are dependent on JAK1 or JAK3 enzyme activity. It has little effect on cytokines involved in hematoepoiesis that are dependent on JAK2. Oclacitinib is not a corticosteroid or an antihistamine.

Pharmacokinetics

In dogs, oclacitinib maleate is rapidly and well absorbed following oral administration, with mean time to peak plasma concentrations (t_{max}) of less than 1 hour. Following oral administration of 0.4-0.6 mg oclacitinib/kg to 24 dogs, the mean (80% confidence limits [CL]) maximum concentration (C_{max}) was 324 (281, 372) ng/mL and the area under the plasma concentration-time curve from 0 to extrapolated to infinity (AUC_{0-inf}) was 1890 (1690, 2110) mg·h/mL. The prandial state of dogs did not significantly affect the rate or extent of absorption. The absolute bioavailability of oclacitinib maleate was 89%.

Oclacitinib has low protein binding with 66.3-69.7% bound in fortified canine plasma at nominal concentrations ranging from 10-1000 ng/mL. The apparent mean (95% CL) volume of distribution at steady-state was 942 (870, 1014) mL/kg body weight.

Oclacitinib is metabolized to the major 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 cytochrome P450 enzymes by oclacitinib is minimal; the inhibitory concentrations (IC_{50}) are 50 fold greater than the observed C_{max} values at the dose used.

Mean (95% CL) total body oclacitinib clearance from plasma was low – 316 (237, 396) mL/h/kg body weight (5.3 mL/min/kg body weight). Following IV and PO administration, the terminal t_{1/2} appeared similar with mean values of 3.5 (2.3, 4.7) and 4.1 (3.1, 5.2) hours, respectively.
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 = 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>0.66</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 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% (23/152) 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 Dermatitis

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: atopic 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 Day 5. 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>
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<tr>
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<td>0.29</td>
<td>&lt;0.0001</td>
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</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.