In 2013, over 400 veterinarians and approximately 1,000 dogs participated in the APOQUEL Early Experience Program. After the program was finished, we surveyed 119 veterinarians and 356 dog owners. Their feedback was overwhelmingly positive.\textsuperscript{1,2}
99% of veterinarians surveyed would recommend APOQUEL to other veterinarians.¹

96% of veterinarians were satisfied with the efficacy of APOQUEL¹

“So far, much less itching. Hardly any, if at all. I’m really impressed. Nothing has given this dog relief, ever. Go APOQUEL!” —Dr. Jill Abraham (New York, NY)

98% of veterinarians were satisfied with the speed of onset of APOQUEL¹

“Katie had a pruritic allergy, 10/10 on itch scale, [so we] started her on APOQUEL. After two doses (<24 hours), the owner called in this morning, thanking us profusely. He said the dog is completely different, not itchy, and very happy.” —Dr. Jennifer Blair (Roseville, MN)

91% of veterinarians were satisfied with the side effects of APOQUEL¹

“I have heard from 1 client and she said the dog is a different dog. Pruritus is down 90% and she said the dog is so much more comfortable. I was so glad to hear that.” —Dr. Dale Brown (Fayetteville, NC)

In fact, the majority of veterinarians would prescribe APOQUEL for future acute, seasonal, and chronic cases of pruritus in the next 6 months.¹

Over 75% would replace Novartis’ Atopica® with APOQUEL.

Almost 50% would replace steroids with APOQUEL.
ACCORING TO PET OWNERS WHO HAD DOGS ENROLLED IN THE EARLY EXPERIENCE PROGRAM,

9 OUT OF 10 WOULD RECOMMEND APOQUEL TO A FRIEND.²

PET OWNERS AGREED THAT APOQUEL IMPROVED THE QUALITY OF LIFE

DOG’S LIFE 97%
OWNER’S LIFE 95%

“She loves going for walks. She just has such a different personality than she had before. Or maybe she had that personality but it was just masked by all the pain and suffering before. It’s really great to see how she is now after APOQUEL.” –Owner of Molly

“I wanted to update you on Jenn. The difference in her [since APOQUEL] is amazing. You will never know how much we appreciate everything APOQUEL has done for our dog. It has not only affected our pet but it has affected our lives as well.” –Owner of Jenn
A FAST-ACTING AND SAFE TREATMENT FOR FIRST LINE CONTROL OF CANINE PRURITUS.

**NOVEL**

Uniquely targets the cytokines involved in itch and inflammation with minimal negative impact on immune function.3

**FAST**

Rapid onset of relief within 4 hours. Effectively controls itch within 24 hours.4,5

**SAFE**

Without many of the side effects associated with steroids.5,6

**Indications:** Control of pruritus 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.

For more information, please see full Prescribing Information on next page.

**References:**

All trademarks are the property of Zoetis Inc., its affiliates and/or its licensors, except for Atopica, which is a registered trademark of Novartis AG.
### 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.

### Dosage and Administration
The dose of APOQUEL (oclacitinib maleate) tablets is 0.18 mg/kg (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>
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<td>9.9</td>
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### Indications:
Control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

### 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).

### 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 lump (2.6% APOQUEL, 2.7% placebo), and lethargy (2.0% APOQUEL, 1.4% 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 interdigital furunculosis and 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 subsequent euthanized, including one dog that developed signs associated with a heart base mass after 60 days of APOQUEL administration. One of the 147 dogs in the placebo group developed a Grade I mast cell tumor after 60 days of APOQUEL administration. All of these 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.

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 222 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).

### 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. 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 JAK2. Oclacitinib is not a corticosteroid or an antihistamine.

### Animal Safety
For oral use in dogs only

#### Dosage 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.

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### References
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/AnimalVets/safetyhealth](http://www.fda.gov/AnimalVets/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 hematopoiesis that are dependent on JAK1 or JAK3. 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 (Tmax) 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 (Cmax) was 324 (281, 372) ng/mL, and the mean area under the plasma concentration-time curve from 0 and extrapolated to infinity (AUCinf) was 1690 (1690, 2110) ng-h/mL. The prandial state of dogs does 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.

### Animal Safety
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-butenedicarboxylate. The chemical structure of oclacitinib maleate is:

![Chemical Structure of Oclacitinib Maleate](image_url)
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 cytochrome P450 enzymes by oclacitinib is minimal; the inhibitory concentrations (IC50) are 50 fold greater than the observed Cmax values at the use dose.

Mean (95% CI) total body oclacitinib clearance from plasma was low – 316 (237, 396) mL/min/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 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, Allergic Dermatitis**

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>APOQUEL (n = 131)</th>
<th>Placebo (n = 133)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owner-Assessed Pruritus VAS Treatment Success</td>
<td>0.86</td>
<td>0.04</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Veterinarian-Assessed CADESI Treatment Success</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 Veterinarian-assessed CADESI scores (on Days 14 and 28) were lower (improved) in dogs in the APOQUEL group. By Day 30, 86% (71/84) 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 72.

**Control of Pruritus Associated with Atopic 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 atopic dermatitis attributed to one or more of the following conditions: atopic dermatitis, flea allergy, food allergy, contact allergy, and/or unspecified atopic 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.

** Estimated Proportion of Dogs with Treatment Success**

<table>
<thead>
<tr>
<th>Effectiveness Parameter</th>
<th>APOQUEL</th>
<th>Placebo</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 Veteraninarian-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**

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 dogs in the high dose (3X and 5X) treatment groups, dosed at 1.8 mg/kg oclacitinib (3X maximum exposure dose) twice daily for 84 days. For 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 (CPV) <80% (9 of 8) of the dogs achieved adequate serologic response. Clinical observations 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-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 pneumonia of short duration and evidence of chronic lymphadenitis of mesenteric lymph nodes. During the three month recovery phase to this study, one oclacitinib maleate-treated dog (32-weeks old) was euthanized on Day 28 due to clinical signs which included enlarged prescapular lymph nodes, bilateral exophora, lethargy, mild dyspnea, and fever. The dog showed an elevated white blood cell (WBC) count. Necropsy revealed lesions consistent with sepsis secondary to immunosuppression. Bone marrow hyperplasia was consistent with response to sepsis.

**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).

**Distributed by**: Zoetis Inc.
Kalamazoo, MI 49007

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