WHEN CLIENTS CALL, ARE THEIR ITCHY DOGS GETTING FAST RELIEF FROM ALLERGIC ITCH?

It would be a shame to make them wait

www.ScienceOfStrongerBonds.com
www.apoquel.com
Making them wait for relief:

- **Erodes the cherished bond** between the pet and client
- Impacts the client’s relationship with the veterinarian
- Prevents pet owners from getting what they want: real relief for their pet instead of treatments they can try at home

- **88% have already tried at-home itch treatments** (up to 15) before bringing their dog to the clinic¹

According to a recent nation-wide phone survey, **7 out of 10** clients with itchy dogs, who call the practice looking for relief, get a phone fix instead of a recommendation to make an appointment with the veterinarian.²

**PHONE FIXES SHARED BY CLINIC TEAMS FOR ITCHY DOG RELIEF**

- Pick up an antihistamine²
- Give a bath
- Put on a T-Shirt
- Change the food
- Look for fleas

“**They wanted me to bathe him in an oatmeal bath once a week and bathe him in medicated shampoo. He also recommended that I give my dog Benadryl and vitamins.**”² — Client

**International Committee on Allergic Diseases of Animals (ICADA) Guidelines³**

Interventions likely to be of **little or no benefit** to treat acute flares of canine atopic dermatitis: **Antihistamines**

“**Antihistamines might provide a small and limited benefit in some dogs with atopic dermatitis**”

**3 of 10** receive a recommendation to schedule an exam with the veterinarian.²

The shortest distance between itch and relief is a straight line to an exam with the DVM and APOQUEL® for fast, safe relief from allergic itch.
COMMIT TO STOP ALLERGIC ITCH WITH APOQUEL FIRST LINE, EVERY TIME

- Provides rapid itch relief within 4 hours, protecting the bonds that matter most
- Targets itch and inflammatory cytokines resulting in significant reduction of pruritus and inflammation
- Can be used long-term with many other medications, including NSAIDs, anti-infectives, parasiticides, antifungals and allergen-specific immunotherapy
- Allows flexibility to stop and start control of pruritus quickly, as necessary, for assessments during the diagnostic work-up (e.g. flea and food trials)

*The use of APOQUEL has not been evaluated in combination with other systemic immunosuppressants, such as corticosteroids and cyclosporine.

#1 GOAL Get itchy dogs the relief they need by getting them off the rollercoaster and into your clinic for an exam.

Take care to address each step of the itchy dog's journey with your practice.

Post a version at each phone, holding each other accountable for NO phone fixes! --many of which clients already found on Dr. Google!

Practice and plan for the questions you may get from clients over the phone
(Tip: have the veterinarian play the role of the patient care coordinator who answers the phone so the team can hear how common client questions should be answered)

Ms. Smith: "What can I do for Max at home?"
Patient Care Coordinator: "Mrs. Smith, I know we both want relief for Max ASAP. Over-the-Counter products aren't often effective or they may represent just one part of a potential treatment plan for Max’s itch. Dr. Green can make a recommendation for fast, safe, effective relief and can even administer the first dose in the exam room. Let’s get Max scheduled for Dr. Green’s first available appointment so we can find out why he is so itchy."

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.

References:
**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 (22)-2-butenedicarboxylic acid. 

The chemical structure of oclacitinib maleate is:

![Chemical Structure of Oclacitinib Maleate](image)

**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/lb 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.

**Dosage 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>3.4</td>
</tr>
<tr>
<td>10.0</td>
<td>14.9</td>
<td>-</td>
</tr>
<tr>
<td>15.0</td>
<td>19.9</td>
<td>-</td>
</tr>
<tr>
<td>20.0</td>
<td>29.9</td>
<td>-</td>
</tr>
<tr>
<td>25.0</td>
<td>35.9</td>
<td>-</td>
</tr>
<tr>
<td>30.0</td>
<td>44.9</td>
<td>-</td>
</tr>
<tr>
<td>45.0</td>
<td>69.9</td>
<td>-</td>
</tr>
<tr>
<td>60.0</td>
<td>89.9</td>
<td>-</td>
</tr>
<tr>
<td>90.0</td>
<td>129.9</td>
<td>-</td>
</tr>
<tr>
<td>130.0</td>
<td>175.9</td>
<td>-</td>
</tr>
</tbody>
</table>

**Warnings:**

- **APOQUEL** is not for use in dogs less than 12 months of age (see Animal Safety).
- **Precautions:** APOQUEL is not for use in dogs with IBD or IBD-related dermatitis.
- **Adverse Reactions:** Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplastic conditions (see Adverse Reactions and Animal Safety).

**Mechanisms of Action:**

- Oclacitinib inhibition of the function of pre-existing T helper cells, including T helper cells involved in hematopoiesis that are dependent on JAK2.
- Oclacitinib has little effect on cytokines involved in allergy that are dependent on JAK1 or JAK3.
- Oclacitinib decreases the expression of cytokines involved in dermatitis that are dependent on the inhibition of JAK1 and JAK3.

**To report suspected adverse events,** contact Zoetis Inc. at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

**Clinical Pharmacology:**

- **Mechanisms of Action:** Oclacitinib inhibits the function of pre-existing T helper cells, including T helper cells involved in hematopoiesis 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 mean area under the plasma concentration-time curve from 0 and extrapolated to infinity (AUC_{0-Inf}) was 1890 (1690, 2110) ng·hr/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 66.3-68.7% 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 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 excretion. 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 use dose.

- Mean (95% CL) total body oclacitinib clearance from plasma was low – 316 (237, 398) 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 3.2 (2.4, 4.7) and 4.1 (3.1, 5.2) hours, respectively.

**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 112-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 (23.4% APOQUEL, 19.8% placebo), vomiting (23.0% APOQUEL, 14.2% 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 of areas of skin and fur (1 dog); diarrhea (1 dog); fever, lethargy and cystitis (1 dog); an infiltrated footpad and vomiting (1 dog); and diarrhea, vomiting, and lethargy (1 dog). Dogs in the APOQUEL group had a slight decrease in mean white blood cell counts (WBC) and neutrophil counts compared to the placebo group, with group means remaining 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.

**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 APOQUEL at least once dose of APOQUEL. Of these dogs, four dogs from study due to suspected non-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 demodicidosis 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 an acute lung 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 urorhitis (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-specified dental lumps (12.0%), otitis (9.9%), vomiting (9.2%), diarrhea (6.6%), hives (5.0%), pruritus (5.0%), anorexia (3.5%), lethargy (2.8%), yeast skin infections (2.5%), and neutropenia (2.1%). Polydipsia (1.4%), lymphopenia (1.1%), nausea (1.1%), increased appetite (1.1%), aggression (1.1%), and weight loss (0.7%).
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</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owner-Assessed Pruritus VAS</td>
<td>0.66 (n = 131)</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>
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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, 86.6% (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.

Owner-Assessed Pruritus VAS Treatment Success, Allergic Dermatitis

Effectiveness Parameter | APOQUEL | Placebo | P-value |
<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Estimated Proportion of Dogs with Treatment Success</td>
<td>0.67 (n = 203)</td>
<td>0.29 (n = 204)</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 (3X maximum exposure dose), 1.8 mg/kg (3X, 8 dogs), and 3.0 mg/kg (6X, 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 (crypts) 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 lymphadenopathy of peripheral nodes. Microscopic findings considered to be oclacitinib maleate-related included decreased cellularity (lymphohistiocytic) 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 parainfluenza virus (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 node, interdigital furunculosis, crypts, 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 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-week-old) was euthanized on Day 28 due to clinical signs which included enlarged prescapular lymph nodes, bilateral epiphora, 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.

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 dermecte 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.

NADA #141-345, Approved by FDA
Made in Italy

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