Oclacitinib

- (ok-la-sit-ti-nib)
- **Apoquel®**
- **Janus Kinase (JAK) Inhibitor, Antipruritic**

**Prescriber Highlights**

- JAK1 & JAK3 inhibitor for treating pruritus in dogs.
- New drug so full adverse effect profile is unknown. Most commonly reported adverse effects are gastrointestinal related (vomiting, diarrhea, inappetence), polydipsia, and lethargy. Serious adverse effects including susceptibility to infections (e.g., pneumonia, demodicosis), neoplasia, and skin disorders are possible.
- Dosed twice a day for up to 2 weeks and then backed down to once daily.

**Uses/Indications**

Oclacitinib is FDA-approved in dogs (at least 1-year old) for the control of pruritus associated with allergic dermatitis and control of atopic dermatitis (Anon 2013a).

In a large (436 dogs), randomized, double-blinded, placebo-controlled, pre-authorization study evaluating the safety and efficacy of oclacitinib for the control of pruritus associated with allergic dermatitis, both owner- and veterinarian-scored visual analog scale scores for pruritus were significantly better for oclacitinib treated dogs versus those treated with placebo (Cosgrove et al. 2013a). Another similar study in 299 dogs with chronic atopic dermatitis found that when compared to the placebo group, treated dogs had significantly higher reductions in VAS scores (owner-scored) and Canine AD Extent and Severity Index (CADESI-02; dermatologist-scored) (Cosgrove et al. 2013b).

**Pharmacology/Actions**

Oclacitinib inhibits Janus kinase (JAK) 1-dependent and JAK3-dependent cytokines, including interleukin (IL)-2, IL-4, IL-6 IL-13, and IL-31. These cytokines are thought to play a significant role in inflammatory, pruritic, and allergic processes. Oclacitinib does not significantly inhibit JAK2-dependent cytokines that are important for hematopoiesis.

Onset of antipruritic efficacy can be noted within 12 hours of the first dose.

**Pharmacokinetics**

After oral administration to dogs, oclacitinib maleate has a bioavailability of 89% and peak plasma concentrations occur in less than 1-hour. Feeding state did not affect pharmacokinetics. Oclacitinib is not significantly bound to plasma proteins in dogs (66-69%). Apparent volume of distribution
(steady-state) was 942 mL/kg and total body plasma clearance was 5.3 mL/min/kg. Terminal half-life is 3.5 hours (IV) and 4.1 hours (PO). Oclacitinib is metabolized to several metabolites with an oxidative form being the major metabolite. Less than 4% of the drug is excreted unchanged in the urine within 24 hours of dosing (Collard et al. 2012a; Collard et al. 2012b).

CONTRAINDICATIONS/Precautions/Warnings
The product label states that it is not for use in dogs <12 months of age, those with serious infections, breeding dogs, or pregnant or lactating bitches. Additionally, oclacitinib is labeled that it may increase susceptibility to infection, including demodicosis, and exacerbate neoplastic conditions (Anon 2013a).

While not stated on the label, marketing information from the drug sponsor states that oclacitinib has been safely used in conjunction with vaccines (Anon 2013b). A pre-authorization vaccine response study concluded that at 3X (1.8 mg/kg) doses, there were adequate serological immune responses to a multivalent modified live vaccine (MLV) containing canine distemper virus (CDV), canine parvovirus (CPV), canine adenovirus (CAV), and canine parainfluenza virus (CPI), and to a killed-virus rabies vaccine. However at this dosage rate, 5 of 8 treated dogs developed enlarged lymph nodes, interdigital furunculosis, cysts and mild to severe pododermatitis. One dog was euthanized and was found to have had acute pneumonia and chronic lymphadenitis of mesenteric lymph nodes (Anon 2013c).

Adverse Effects
Due to its recent approval and limited clinical use, oclacitinib’s adverse effect profile is not fully known. Most commonly gastrointestinal effects (vomiting, diarrhea, anorexia), polydipsia or lethargy have been noted but other potentially serious adverse effects, including susceptibility to infections (e.g., pneumonia, demodicosis), neoplasia, and skin disorders are possible.

Reproductive/Nursing Safety
Safe use during pregnancy, breeding or nursing has not been established. The drug’s label states that it should not be used in breeding dogs, or pregnant or lactating bitches.

Overdosage/Acute Toxicity
Limited information is available on acute toxicity. In pre-approval margin of safety studies, dogs receiving 5X dosages (3 mg/kg PO twice daily for 6 weeks, then once daily for 20 weeks) clinically observed adverse effects attributable to the drug included vomiting, diarrhea, interdigital furunculosis/dermatitis, papillomas and peripheral node lymphadenopathy. No deaths or serious effects were reported (Anon 2013c).

Drug Interactions
No specific drug interactions have been reported. The package insert states that use has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic
immunosuppressive agents. Oclacitinib is not highly bound to plasma proteins and does not inhibit canine cytochrome P450 enzymes. Marketing information from the drug sponsor states that oclacitinib has been safely used in conjunction with other common medications including vaccines, NSAIDs, antibiotics, parasiticides, anticonvulsants, and allergen immunotherapy (Anon 2013b), but this information could not be found on the drug label.

**Laboratory Considerations**

- Marketing information from the drug sponsor states that oclacitinib can be used in combination with allergy testing (Anon 2013b), but this information could not be found on the current drug label.

**Dosages**

**Dogs:**

- For the control of pruritus associated with allergic dermatitis and control of atopic dermatitis (labeled-dose; FDA-approved): 0.4 – 0.6 mg/kg PO twice daily for up to 14 days, and then once daily for maintenance therapy. May be administered with or without food. A dosing chart showing the appropriate number and size of tablets to be administered for the dog’s bodyweight can be found in the package insert. (Adapted from Label Information: Apoquel®)

**Monitoring**

- Clinical efficacy.
- Monitor for the development of infections, including demodicosis, and neoplasia.

**Client Information**

- For use in dogs only; not for human use. 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 (Anon 2013a).
- May give with or without food. If dog vomits or acts ‘sick’ after a dose, try giving with some food.
- If your dog shows signs of infection, pneumonia (e.g., difficulty breathing or is listless) or has a fever, contact your veterinarian immediately.
- If you see abnormal skin changes or growths, contact your veterinarian.

**Chemistry/Synonyms**
Oclacitinib maleate (CAS Registry 1208319-26-9; ATC:QD11AH90) is a synthetic sulfonamide-derivative inhibitor of Janus Kinase (JAK).

Oclacitinib may also be known as PF-03394197-11. The trade name is Apoquel®.

**STORAGE/STABILITY**

Tablets should be stored at room temperature (20-25°C; 68-77°F). Excursions are allowed between 15-40°C (59-104°F).

**COMPATIBILITY/COMPOUNDING CONSIDERATIONS**

No specific information noted.

**DOSE FORMS/REGULATORY STATUS**

**Veterinary-Labeled Products:**

Oclacitinib Oral Tablets (scored): 3.6 mg, 5.4 mg, & 16 mg; Apoquel®; (Rx). Approved for use in dogs (NADA 141-345).

**Human-Labeled Products: None.**

**REVISIONS/REFERENCES**

Monograph written August 2013; revised May 2014.


Cosgrove, S. B., et al. (2013a). Efficacy and safety of oclacitinib for the control of pruritus and associated skin lesions in dogs with canine allergic dermatitis. *Veterinary Dermatology* n/a-n/a.