Dogs that withdrew from the masked field study were monitored for the next 3 months. 

**Mechanism of Action**

Oclacitinib is a synthetic Janus Kinase (JAK) inhibitor. JAKs are a family of enzymes that play an important role in the body's immune response. Oclacitinib inhibits specific JAK enzymes involved in hematopoiesis that are cytokines involved in hematopoiesis.

**Pharmacokinetics**

In dogs, oclacitinib maleate is rapidly and well absorbed following oral administration. Following oral administration, the mean observed peak plasma concentration (Cmax) was 942 (870, 1014) mL/kg body weight. Oclacitinib is extensively metabolized by a combination of the liver and the gut and is recovered in the urine as metabolites that are more polar than the parent compound. The terminal elimination half-life of oclacitinib was 3.8-4.1 hours.

**Adverse Reactions and Animal Safety**

**Human and Animal Safety:** 12-months of APOQUEL administration to dogs of age range 12 months to 8 years in weight range 2-30 kg. APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety, 12 months of age).

**Representative Adverse Reactions**

In dogs, the following adverse reactions were reported in clinical studies and/or have been reported in animals treated with oclacitinib:

- Ocular: transient conjunctival hyperemia, transient corneal keratitis
- Dermatological: alopecia, pruritus, dermatitis, eczema, hair coat change, rash, seborrhea, dermatitis simplex, pruritic dermatitis
- Gastrointestinal: anorexia, nausea, vomiting, diarrhea, flatulence, constipation, reduced appetite
- Neuromuscular and skeletal: fasciculations, muscle atrophy
- Other: labored breathing, lower respiratory infection, urinary tract infection

**Pharmacodynamic Effects**

The dose of APOQUEL was 0.4-0.6 mg/kg per dose twice daily for 28 days (range 1 to 610 days). Of these, 286 days of APOQUEL administration, two dogs each developed an anal sac (one dermal, one anal sac) after approximately 210 and 320 days of APOQUEL administration. One dog developed low grade B-cell lymphoma after 392 days of APOQUEL administration. Two dogs each developed an intracranial neoplasms, and transitional cell carcinoma.

**Compliance:**

APOQUEL tablets are supplied in white, oval-shaped tablets, and are supplied in bottles of 30 tablets.

The dog showed an elevated white blood cell count with evidence of chronic lymphadenitis of mesenteric lymph nodes. During the three month recovery phase to this study, one oclacitinib maleate-treated dog (3X maximum exposure dose) twice daily for 84 days. For dogs that were administered oclacitinib for 26 weeks. Eight dogs received placebo (empty gelatin capsule) at the same dosage schedule. Clinical observations that were considered likely to be oclacitinib-related included mild, dose-dependent increases in the number and frequency of whites/lymphocytes (WBC) in one or more blood parameters. Microscopic findings considered to be oclacitinib-related included increased lymphoid hyperplasia of mesenteric lymph nodes, enlarged prescapular lymph nodes, and chronic active inflammation was seen in the interdigital furunculosis. In addition, 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 the feet) and lymphadenopathy of peripheral lymph nodes. Microscopic findings considered to be oclacitinib-related included lymphoid hyperplasia of mesenteric lymph nodes. Microscopic findings considered to be oclacitinib-related included dermatitis and decreased cellularity (lymphoid) in Gut-Associated Lymphoid Tissue (GALT), spleen, lymph nodes draining feet affected with interdigital furunculosis. Five oclacitinib maleate-treated dogs had microscopic evidence of interdigital furunculosis. Lymphoid hyperplasia was consistent with response to conversion in the leukocyte subsets of lymphocytes, granulocytes, and monocytes. Lymphoid hyperplasia was consistent with response to treatment. The dog showed an elevated white blood cell count (WBC) on Day 28 due to clinical signs which included epiphora, lethargy, mild dyspnea, and fever. Necropsy revealed lesions of pneumonia of short duration and evidence of frank blood in stool.

The treated dog (32-weeks old) was euthanized on Day 74 after physical examination revealed the dog to be febrile, lethargic, with pale mucous membranes and decreased frequency of interdigital furunculosis (cysts) on one or more feet during the study. 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 the feet) and lymphadenopathy of peripheral lymph nodes. Microscopic findings considered to be oclacitinib-related included lymphoid hyperplasia of mesenteric lymph nodes. Microscopic findings considered to be oclacitinib-related included lymphoid hyperplasia.