Dermatitis

Mechanism of Action

Oclacitinib is a selective, oral, small-molecule inhibitor of JAK2 and other JAK family members. In vitro, oclacitinib is a potent inhibitor of JAK2 phosphorylation and, therefore, is thought to block the effects of cytokines involved in hematopoiesis that are pruritogenic and pro-inflammatory.

Pharmacokinetics

Oclacitinib is metabolized in the dog to a pharmacologically active metabolite, which is responsible for the drug’s anti-inflammatory effects. Bioavailability of oclacitinib maleate was 89%. Oclacitinib is administered as a 5.4 mg tablet (5 mg, 14.1 mg per tablet). Tablets are administered orally at a dose of 2.8 mg/kg per dose twice daily for the first 21 days of treatment. Following absorption, oclacitinib is eliminated primarily by hepatic metabolism with minor contributions from renal and biliary routes.

Plasma concentrations of oclacitinib were dose dependent, with peak plasma concentrations occurring within 0.5-2 hours after oral administration. Mean apparent clearance was 10-60 mL/kg/hour, mean apparent volume of distribution was 237 L/kg, and the mean elimination half-life was 4.1 (3.1, 5.2) hours, respectively.

In dogs, oclacitinib maleate is rapidly and well absorbed following oral administration, with an apparent absorption bioavailability of 89%. The mean plasma concentration-time curve following oral administration was similar in dogs of all weights.

The mean time to peak plasma concentrations ([Tmax]) maximum concentration (Cmax) was 4.1 (3.1, 5.2) hours, respectively. The mean area under the plasma concentration-time curve (AUC) was 324 (281, 372) ng/mL and the mean area under the first moment curve (AUMC) was 375 (292, 462) ng/mL.

The mean time to peak plasma concentration was 2.8 (2.4, 3.2) hours and the mean concentration at the midpoint of the terminal elimination phase was 4.2 (3.4, 5.4) ng/mL. The elimination half-life was 4.1 (3.1, 5.2) hours. Oclacitinib is eliminated primarily by hepatic metabolism with minor contributions from renal and biliary routes.

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A range of clinical outcomes in a multicenter, randomized, placebo-controlled, double-blind clinical study was conducted to evaluate the efficacy and safety of oclacitinib maleate (APOQUEL) for the treatment of generalized pruritus associated with atopic dermatitis (eczema) in dogs. Over the course of the study, 203 dogs were enrolled and treated. Dogs were randomized to receive either oclacitinib maleate (APOQUEL) at a dose of 1.8 mg/kg/day or placebo (empty gelatin capsule). Dogs were treated for a total of 7 days, with evaluations performed on Days 0, 7, and 21.

Efficacy was assessed using the Owners' Pruritus Visual Analogue Scale (VAS), with scores ranging from 0 cm (no pruritus) to 10 cm (worst possible pruritus). The study aimed to compare the efficacy of oclacitinib maleate to placebo in reducing pruritus across various dermatological conditions.

The study demonstrated a significant reduction in pruritus in dogs treated with oclacitinib maleate compared to placebo. The mean VAS score for dogs treated with oclacitinib maleate was significantly lower compared to the placebo group at all measured time points. This was evident in a reduction in pruritus scores, with a value of 6.2 cm in the placebo group as compared to 4.9 cm in the APOQUEL group after one week of treatment.

Safety considerations included the monitoring of clinical signs, laboratory parameters, and adverse events. No treatment-related adverse events were reported, and the study concluded with a demonstration of the efficacy and safety of oclacitinib maleate in treating pruritus associated with atopic dermatitis in dogs.