For the use only of a Veterinary Practitioner, Hospital or Laboratory

ELOFI-PET

Oclacitinib Maleate Tablets 5.4 / 16mg tablets

Warning: To be sold by the retail on the prescription of a veterinarian only

Statement of active Substance:
Composition:
Oclacitinib maleate Tablets 5.4mg
Each tablet contains:

Oclacitinib maleate	5.4mg
Excipients	Q.S.

Oclacitinib maleate Tablets 16mg
Each tablet contains:

Oclacitinib maleate	16mg
Excipients	Q.S.

Pharmaceutical form: Film-coated scored tablet

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 recommended dose of ELOFI-PET tablets is 0.4 to 0.6 mg oclacitinib/kg body weight, administered orally, twice daily for up to 14 days, and then tapered down to once daily for maintenance therapy. Oclacitinib may be administered with or without food.

Warnings:
ELOFI-PET is for veterinary use and in treatment of dogs only. 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.
ELOFI-PET is not for use in dogs less than 12 months of age.
ELOFI-PET is an immunomodulator and is not for use in dogs with serious infections and those susceptible to infections such as demodicosis. ELOFI-PET may exacerbate neoplastic conditions.
In dogs with a history of recurrent serious infections or recurrent demodicosis or neoplasia, consider the risks and benefits of treatment prior to initiating ELOFI-PET.
Keep ELOFI-PET out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions:
Dogs receiving ELOFI-PET should be monitored for the development of infections, including demodicosis, and neoplasia. The use of Oclacitinib maleate has not been evaluated in combination with cyclosporine, or other systemic immunosuppressive agents.
ELOFI-PET is not for use in breeding dogs, or pregnant or lactating bitches.

Dosage Chart:

Weight Range in kg		Minimum dose	Maximum dose	Dosage to be administered (as number of tablets)	
High	**Low**	**0.4mg/kg**	**0.6mg/kg**	**5.4mg**	**16mg**
4.5	5.9	1.8	2.7	½	
6	8.9	2.4	3.6		
9	13.4	3.6	5.4	1	
13.5	19.9	5.4	8.1		½
20	26.9	8	12	2	
27	39.9	10.8	16.2		1
40	54.9	16	24		1½
55	80	22	33		2

Adverse Reactions:
Diarrhea, vomiting, anorexia, new cutaneous or subcutaneous lump, lethargy, elevated liver enzymes, dermatitis (i.e. crusts, pododermatitis, pyoderma), seizures, polydipsia, and demodicosis have been reported with use of Oclacitinib in dogs. Benign, malignant, and unclassified neoplasms, dermal masses (including papillomas and histiocytomas), lymphoma and other cancers have also been reported. In most cases, diarrhea, vomiting, anorexia, and lethargy spontaneously resolved with continued dosing. Dogs on Oclacitinib had decreased leukocytes (neutrophil, eosinophil, and monocyte counts) and serum globulin, and increased cholesterol and lipase. However, the mean remained within the normal range. Mean lymphocyte counts were transiently increased at Day 14 of Oclacitinib administration. The following additional clinical signs were reported after beginning Oclacitinib administration: pyoderma, non-specified dermal lumps, otitis, vomiting, diarrhea, histiocytoma, cystitis, anorexia, lethargy, yeast skin infections, pododermatitis, lipoma, polydipsia, lymphadenopathy, nausea, increased appetite, aggression, and weight loss.

Clinical Pharmacology:
Mechanism of Action
Oclacitinib is neither a corticosteroid nor an antihistamine. It inhibits a variety of cytokines that are involved in allergy, pruritus and inflammation that are dependent on JAK1 or JAK3 enzyme activity.

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 (90% 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 (AUC0-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 66.3-69.7% 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. 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 (IC50s) are 50 fold greater than the observed Cmax values at the use dose. Mean (95% CL) total body oclacitinib clearance from plasma was low – 316 (237, 396) mL/h/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 In a double-masked, 112-day, placebo controlled study, dogs were randomized to treatment with Oclacitinib (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 Oclacitinib group compared to the placebo group.

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 Oclacitinib group. By Day 30, 86% (127/147) of the placebo group dogs and 15% (23/152) of the Oclacitinib group dogs withdrew from the masked study because of worsening clinical signs, and had the option to enroll in an unmasked study and receive Oclacitinib. For dogs that continued Oclacitinib 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.

Control of Pruritus Associated with Allergic Dermatitis
In a double-masked, 30-day, controlled study, 436 client owned dogs were enrolled with a history of allergic dermatitis attributed to one or more of the following conditions: atopic dermatitis, flea allergy, food allergy, contact allergy, and other/unspecified allergic dermatitis. Dogs were randomized to treatment with Oclacitinib (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.

After one week of treatment, 86.4% of Oclacitinib 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 Oclacitinib 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 Oclacitinib 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 Oclacitinib treatment beyond one week, the Veterinarian-assessed dermatitis scores continued to improve through study end at Day 30.

Margin of Safety in 12 Month Old Dogs:
Oclacitinib (Apoquel) has a good safety margin in dogs for managing allergies, with a positive benefit/risk profile for long-term use, but high doses (3-5x recommended) in studies caused severe issues like pneumonia and mange, highlighting the need for correct dosing.

Concomitant usage with other drugs and vaccines
Oclacitinib has been demonstrated to be safe when administered concurrently with many common veterinary medications, including various vaccines, antibiotics, and non-steroidal anti-inflammatory drugs (NSAIDs).

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 demodex 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: ELOFI-PET should be stored at room temperature.

How Supplied: ELOFI-PET 5.4mg/16mg is available as strip of 10 tablets and contains oclacitinib maleate 5.4mg and 16mg per tablet respectively.

VETERINARY
NOT FOR HUMAN USE
FOR TREATMENT OF DOGS ONLY

SAVAVET
Shaping the Future

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