SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg Chewable Tablets for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each chewable tablet contains 3.6 mg oclacitinib (as oclacitinib maleate)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets.

Light to dark brown coloured, elongated pentagon shaped, mottled tablets with score lines on both sides. The tablets are debossed in one of the faces with “S S”.

The tablets can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of pruritus associated with allergic dermatitis in dogs.
Treatment of clinical manifestations of atopic dermatitis in dogs.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in dogs less than 12 months of age or less than 3 kg bodyweight.
Do not use in dogs with evidence of immune suppression, such as hyperadrenocorticism, or with evidence of progressive malignant neoplasia as the active substance has not been evaluated in these cases.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals:
Oclacitinib modulates the immune system and may increase susceptibility to infection and exacerbate neoplastic conditions. Dogs receiving Apoquel tablets should therefore be monitored for the development of infections and neoplasia.

When treating pruritus associated with allergic dermatitis with oclacitinib, investigate and treat any underlying causes (e.g. flea allergic dermatitis, contact dermatitis, food hypersensitivity). Furthermore, in cases of allergic dermatitis and atopic dermatitis, it is recommended to investigate and treat complicating factors, such as bacterial, fungal or parasitic infections/infestations (e.g. flea and mange).

Given the potential for effects on certain clinicopathological parameters (see section 4.6), periodic monitoring with complete blood counts and serum biochemistry is recommended when dogs are on long-term treatment.

The tablets are flavoured. In order to avoid accidental ingestion, store tablets in a safe place out of reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after administration.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Ingestion of this product may be harmful for children. To avoid accidental ingestion, administer the tablet(s) to the dog immediately after removal from the blister packaging.

4.6 Adverse reactions (frequency and seriousness)

The common adverse reactions seen up to day 16 of the field trials are listed in the following table:

	Adverse reactions observed in atopic dermatitis study up to day 16		Adverse reactions observed in pruritus study up to day 7	
	Apoquel (n=152)	Placebo (n=147)	Apoquel (n=216)	Placebo (n=220)
Diarrhoea	4.6%	3.4%	2.3%	0.9%
Vomiting	3.9%	4.1%	2.3%	1.8%
Anorexia	2.6%	0%	1.4%	0%
New cutaneous or subcutaneous lumps	2.6%	2.7%	1.0%	0%
Lethargy	2.0%	1.4%	1.8%	1.4%
Polydipsia	0.7%	1.4%	1.4%	0%

After day 16, the following adverse reactions have been observed:
- pyoderma and non-specified dermal lumps have been observed very commonly;

- otitis, vomiting, diarrhoea, histiocytoma, cystitis, yeast skin infections, pododermatitis, lipoma, polydipsia, lymphadenopathy, nausea, increased appetite and aggression have been observed commonly.

Treatment-related clinical pathology changes were restricted to an increase in mean serum cholesterol and a decrease in mean leukocyte count, however, all mean values remained within the laboratory reference range. The decrease in mean leukocyte count observed in oclacitinib-treated dogs was not progressive, and affected all white blood cell counts (neutrophil, eosinophil and monocyte counts) except lymphocyte counts. Neither of these clinical pathology changes appeared clinically significant.

The development of papillomas was noted in a number of dogs in a laboratory study.

Anaemia and lymphoma have been reported very rarely in spontaneous reports.

Regarding susceptibility to infection and neoplastic conditions, see section 4.5.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation, or in breeding male dogs, therefore its use is not recommended during pregnancy, lactation or in dogs intended for breeding.

4.8 Interaction with other medicinal products and other forms of interaction

No drug interactions were observed in field studies where oclacitinib was administered concomitantly with veterinary medicinal products such as endo- and ectoparasiticides, antimicrobials and anti-inflammatories.

The impact of oclacitinib administration on vaccination with modified live vaccines, canine parvovirus (CPV), canine distemper virus (CDV) and canine parainfluenza (CPI) and inactivated rabies vaccine (RV), on 16 week old vaccine naive puppies has been studied. An adequate immune response (serology) to CDV and CPV vaccination was achieved when puppies were administered oclacitinib at 1.8 mg/kg bodyweight (bw) twice daily for 84 days. However, the findings of this study indicated a reduction in serological response to vaccination with CPI and RV in puppies being treated with oclacitinib compared to untreated controls. The clinical relevance of these observed effects for animals vaccinated while being administered oclacitinib (in accordance with the recommended dosing regimen) is unclear.

4.9 Amounts to be administered and administration route

For oral use.

Dosage and treatment schedule:

The recommended initial dose is 0.4 to 0.6 mg oclacitinib/kg bodyweight, administered orally, twice daily for up to 14 days.

For maintenance therapy, the same dose (0.4 to 0.6 mg oclacitinib/kg bodyweight) should then be administered only once a day. The requirement for long-term maintenance therapy should be based on an individual benefit-risk assessment.

Apoquel tablets are chewable, palatable and readily consumed by the majority of dogs.

These tablets can be administered with or without food.

The dosing table below shows the number of tablets required. The tablets are breakable along the score line.

Bodyweight (kg) of dog	**Strength and number of tablets to be administered:**		
	Apoquel 3.6 mg tablets	**Apoquel 5.4 mg tablets**	**Apoquel 16 mg tablets**
3.0–4.4	½		
4.5–5.9		½	
6.0–8.9	1		
9.0–13.4		1	
13.5–19.9			½
20.0–26.9		2	
27.0–39.9			1
40.0–54.9			1½
55.0–80.0			2

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Oclacitinib tablets were administered to healthy, one year old Beagle dogs twice daily for 6 weeks, followed by once per day for 20 weeks, at 0.6 mg/kg bw, 1.8 mg/kg bw and 3.0 mg/kg bw for a total of 26 weeks.

Clinical observations that were considered likely to be related to oclacitinib treatment included: alopecia (local), papilloma, dermatitis, erythema, abrasions and scabbing/crusts, interdigital "cysts", and oedema of the feet.
Dermatitis lesions were mostly secondary to the development of interdigital furunculosis on one or more feet during the study, with the number and frequency of observations increasing with increasing dose. Lymphadenopathy of peripheral nodes was noted in all groups, increasing in frequency with increasing dose, and was frequently associated with interdigital furunculosis.
Papilloma was considered treatment related, but not dose related.

There is no specific antidote and in case of signs of overdose the dog should be treated symptomatically.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Agents for dermatitis, excluding corticosteroids.
ATC vet code: QD11AH90.

5.1 Pharmacodynamic properties

Oclacitinib is a Janus kinase (JAK) inhibitor. It can inhibit the function of a variety of cytokines dependent on JAK enzyme activity. For oclacitinib, the target cytokines are those that are proinflammatory or have a role in allergic responses/pruritis. However, oclacitinib may also exert effects on other cytokines (for example, those involved in host defence or haematopoiesis) with the potential for unwanted effects.

5.2 Pharmacokinetic particulars

Following oral administration in dogs at a dose ranging from 0.55 to 0.9 mg oclacitinib/kg bodyweight, the observed mean C_{max} was 352 ng/ml (ranging from 207 to 860 ng/ml), which occurred at approximately 1.7 hours (t_{max}) post dosing. The half-life ($t_{1/2}$) is 4.8 hours in plasma.

Total body oclacitinib clearance from plasma was low – 316 ml/h/kg bodyweight (5.3 ml/min/kg bodyweight), and the apparent volume of distribution at steady-state was 942 ml/kg bodyweight. Oclacitinib exhibits low protein binding with 66.3% to 69.7% bound in fortified canine plasma at nominal concentrations ranging from 10 to 1,000 ng/ml.

Oclacitinib is metabolised in the dog to multiple metabolites. 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 P450s is minimal, with IC_{50}s 60-fold greater than the observed mean C_{max} (281 ng/ml or 0.833 µM) following 0.6 mg/kg bw oral administration in the target animal safety study. Therefore, the risk of metabolic drug-drug interactions due to oclacitinib inhibition is very low.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pork Liver Powder
Crospovidone (Type A)
Sodium Starch Glycolate (Type A)
Glycerol Monostearate 40-55 (Type II)
Macrogol 3350

Glycerol
Sodium Chloride
Xanthan Gum
Brewer's Yeast, Dried
Silica, Colloidal Anhydrous
Magnesium Stearate

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale in blisters: 2 years.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

Remaining tablet parts should be stored in the blister and be given at the next administration.

6.5 Nature and composition of immediate packaging

The tablets are packaged in aluminium/PVC/Aclar blisters (each strip containing 10 chewable tablets) packed into an outer cardboard box. Pack sizes of 20 or 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 42058/5000

9. DATE OF FIRST AUTHORISATION

24 November 2021

10. DATE OF REVISION OF THE TEXT

November 2021

Approved 24 November 2021