SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg Veterinary film-coated tablets
Apoquel 5.4 mg Veterinary film-coated tablets
Apoquel 16 mg Veterinary film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Active substance:
3.6 mg oclacitinib (as oclacitinib maleate)
5.4 mg oclacitinib (as oclacitinib maleate)
16 mg oclacitinib (as oclacitinib maleate)

Excipients:

Qualitative composition of excipients and other constituents
Tablet core:
Cellulose, microcrystalline
Lactose monohydrate
Magnesium stearate
Sodium starch glycolate
Tablet coating:
Lactose monohydrate
Hypromellose (E464)
Titanium dioxide (E171)
Macrogol 400 (E1521)

White to off-white, oblong shaped film-coated tablets with a score-line on both sides and marked with the letters "AQ" and "S", "M" or "L" on both sides. The letters "S", "M" and "L" refer to the different strengths of tablets: "S" is on the 3.6 mg tablets, "M" on the 5.4 mg tablets, and "L" on the 16 mg tablets.

The tablets can be divided into equal halves.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

3.3 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.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for use in the target species:
Oclacitinib modulates the immune system and may increase susceptibility to infection and exacerbate neoplastic conditions. Dogs receiving the veterinary medicinal product 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 3.6 “Adverse events”), periodic monitoring with complete blood counts and serum biochemistry is recommended when dogs are on long-term treatment.

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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	pyoderma, skin lump, papilloma
Common (1 to 10 animals / 100 animals treated):	lethargy, lipoma, polydipsia, increased appetite nausea, vomiting, diarrhoea, anorexia histiocytoma, fungal skin infection, pododermatitis otitis lymphadenopathy cystitis aggression
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	anaemia, lymphoma, convulsion

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.

Regarding susceptibility to infection and neoplastic conditions, see section 3.5 "Special precautions for use".
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the veterinary medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

3.7 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.

3.8 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.

3.9 Amounts to be administered and administration route

For oral use.

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.

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

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QD11AH90.

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

Following oral administration in dogs, oclacitinib maleate is rapidly and well absorbed, with a time to peak plasma concentration (t_{max}) of less than 1 hour. The absolute bioavailability of oclacitinib maleate was 89%. The prandial state of the dog does not significantly affect the rate or extent of its absorption.

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. Following intravenous and oral administration, the terminal $t_{1/2}$s were similar at 3.5 and 4.1 hours respectively. 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 50-fold greater than the observed mean C_{max} (333 ng/ml or 0.997 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. No accumulation was observed in the blood of dogs treated for 6 months with oclacitinib.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

The expiry date of the product is indicated on the packaging materials. The expiry date refers to the last day of that month.
Shelf-life after opening the bottle: 42 days
Any remaining half tablets should be discarded after 3 days.

5.3 Special precautions for storage

Store below 25 °C.
Any remaining half tablet should be placed back in the in the HDPE bottle (for a maximum of 3 days).

5.4 Nature and composition of immediate packaging

All tablets strengths are packaged in white HDPE plastic bottle with child resistant closure. Pack sizes of 100 tablets.

Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials from such veterinary medicinal products should be disposed of as a toxic waste. Do not dispose of in the sewage system.

6. MARKETING AUTHORISATION HOLDER

Zoetis Israel Holding B.V. 5 Atir Yeda Street, Kfar Saba, Israel

7. MARKETING AUTHORISATION NUMBER(S)

Apoquel 3.6 mg Veterinary 157-48-34524-00, 157-48-34524-01
Apoquel 5.4 mg Veterinary 157-49-34536-00, 157-49-34536-01
Apoquel 16 mg Veterinary 157-50-34535-00, 157-50-34535-01

8. MANUFACTURER

ZOETIS LLC (SUBSIDIARY OF ZOETIS INC), USA, 2605 EAST KILGORE ROAD, KALAMAZOO, MICHIGAN 49001, USA
Or
PFIZER ITALIA S.R.L, ITALY, LOCALITA MARINO DEL TRONTO, 63100 ASCOLI PICENO (AP), ITALY

9. DATE OF REVISION OF THE TEXT

Revised in August 2024 according to MOH guideline