CONSUMER PACKAGE INSERT FOR A VETERINARY PREPARATION

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved

The medicine is dispensed with a veterinarian's prescription only

For animal use only

1. NAME, FORM AND STRENGTH OF THE VETERINARY MEDICINE

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

2. ACTIVE INGREDIENT

Each film-coated tablet contains:
Apoquel 3.6 mg veterinary tablets
3.6 mg oclacitinib (as oclacitinib maleate)
Apoquel 5.4 mg veterinary tablets
5.4 mg oclacitinib (as oclacitinib maleate)
Apoquel 16 mg veterinary tablets
16 mg oclacitinib (as oclacitinib maleate)
The list of inactive ingredients is in section 13.

3. WHAT IS THE MEDICINE INTENDED FOR?

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

4. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active ingredient or to any of the ingredients of the preparation.
Do not use in dogs under 12 months of age or that weigh less than 3 kg.
Do not use in dogs that present immunosuppression, such as hyperadrenocorticism, or if there is evidence of advanced malignant neoplasia, since the active ingredient has not been evaluated in these cases.

5. SIDE EFFECTS

The common side effects observed up to day 16 in field studies are listed in the table.

	Side effects observed in atopic dermatitis study up to day 16		Side effects observed in pruritus study up to day 7	
	APOQUEL (n=152)	Placebo (n=147)	APOQUEL (n=216)	Placebo (n=220)
Diarrhea	4.6%	3.4%	2.3%	0.9%
Vomiting	3.9%	4.1%	2.3%	1.8%
Loss of appetite (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 side effects have been observed: pustular dermatitis (pyoderma) and non-specified dermal lumps are very common effects. Otitis, vomiting, diarrhea, benign tumor (histiocytoma), cystitis, yeast skin infections, inflammation on the soles of the feet (pododermatitis), benign tumor in the fat tissue (lipoma), polydipsia, enlarged lymph nodes (lymphadenopathy), nausea, increased appetite and aggression are common effects.
Treatment-related pathological clinical changes only included an increase in mean serum cholesterol level and a decrease in mean leukocyte count, however, all values remained within the normal range. The observed decrease in leukocyte count in oclacitinib-treated dogs was not progressive, and affected all white blood cell counts (neutrophils, eosinophils and monocytes), except lymphocytes. None of these pathological changes had a clinically significant effect.
In a laboratory study, the development of papillomas was documented in a number of dogs.
Anemia and lymphoma have been reported very rarely in spontaneous reports.

If you notice any severe side effects or side effects not mentioned in this leaflet, inform the attending veterinarian.
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects,
or by entering the link:
https://sideeffects.health.gov.il/

6. TARGET SPECIES

Dogs

7. METHOD OF ADMINISTRATION AND DOSAGE

For oral administration.

Dosage and treatment schedule
The recommended initial dosage is 0.4-0.6 mg oclacitinib per kg bodyweight, administered orally, twice a day for up to 14 days.
For maintenance therapy (after the first 14 days of treatment), the same dosage (0.4-0.6 mg oclacitinib per kg bodyweight) should then be administered only once a day. Long-term treatment should be based on an individual benefit-risk assessment.
The tablets can be administered with or without food.
The number of tablets can be determined according to the table below. The tablets can be halved along the score line.

Body weight (kg) of dog	Dosage and number of tablets to be administered		
	APOQUEL veterinary 3.6 mg	APOQUEL veterinary 5.4 mg	APOQUEL veterinary 16 mg
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

8. HOW TO USE THE PREPARATION

Dogs should be carefully observed following administration to ensure that it swallowed the tablet.

9. WITHDRAWAL PERIOD

Not applicable.

10. WARNINGS

• Special warnings relating to safety of use of the medicine in animals

Oclacitinib modulates the immune system and therefore, may increase susceptibility to infections and exacerbate neoplastic conditions. Dogs taking Apoquel should therefore be monitored for the development of infectious diseases and neoplasia.
When treating pruritus associated with allergic dermatitis with oclacitinib, investigate and treat the underlying cause, if any (e.g., dermatitis caused by a flea allergy, contact dermatitis, food hypersensitivity). Furthermore, in cases of allergic or atopic dermatitis, it is recommended to investigate and treat factors that may exacerbate the condition, such as: bacterial or fungal infections or ectoparasitic infestations (e.g., fleas and mange).
Since the preparation may cause certain clinicopathological effects (see section 5), it is recommended that dogs on long-term treatment be monitored by means of a complete blood count and biochemistry.

• Special warnings relating to the safety of the person administering the preparation

Wash hands upon completion of use.
If the preparation was accidentally swallowed, seek medical assistance immediately and show the package leaflet or label of the preparation to the doctor.

• Pregnancy and lactation

The safety of the veterinary preparation has not been tested in pregnant or lactating animals, or in breeding male dogs; therefore, it is not recommended for use during pregnancy, lactation or in dogs intended for breeding.

• Interactions with other medicines and other forms of interactions

No interactions were observed in field studies where oclacitinib was administered concomitantly with other veterinary preparations such as endo- and ectoparasiticides, antibiotics or anti-inflammatories.
The impact of oclacitinib administration on live vaccinations: canine parvovirus (CPV), canine distemper virus (CDV) and canine parainfluenza (CPI) and the inactivated rabies vaccine (RV), on 16-week-old puppies that were not previously immunized, has been studied. An adequate immune response (in serological terms) to CDV and CPV vaccinations was achieved when puppies were administered an oclacitinib dosage of 1.8 mg/kg bodyweight twice a day for 84 days. However, the findings of this study indicated a reduction in the serological response to vaccinations with CPI and RV in puppies treated with oclacitinib, as compared to untreated controls. The clinical significance of the findings in animals vaccinated during the course of treatment with oclacitinib (in accordance with the recommended dosing regimen) is unclear.

• Overdose

Oclacitinib tablets were administered to healthy, one-year-old Beagle dogs, twice a day for 6 weeks, followed by once a day for 20 weeks, at a dosage of 0.6 mg per kg bodyweight, 1.8 mg per kg bodyweight and 3.0 mg per kg bodyweight for a total of 26 weeks.
Clinical effects that were considered highly likely to be related to oclacitinib treatment included: local alopecia, papilloma, dermatitis, erythema, abrasions and scabbing, interdigital "cysts" and oedema of the feet.
Inflammatory skin lesions were mostly secondary to the development of interdigital furunculosis on one or more feet during the study, with their number and frequency increasing with increasing dose. Lymphadenopathy of peripheral lymph nodes was noted in all groups, increasing in frequency with increasing dose, and was frequently associated with interdigital furunculosis.
Papilloma was found to be treatment related, but not dose related.
There is no specific antidote for the preparation. In case of overdose, symptoms should be symptomatically treated.

• Incompatibility

Unknown

11. STORAGE INSTRUCTIONS

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning.
- Do not use the medicine after the expiry date (exp. Date) that appears on the package. The expiry date refers to the last day of that month.
- Storage conditions below 25°C.
- Shelf-life after opening the bottle: 42 days
- Shelf-life after breaking the tablet: 3 days

Store half-tablets in the original package

12. INSTRUCTIONS REGARDING DISPOSAL OF THE PREPARATION/REMNANTS OF THE PREPARATION AFTER USE

All veterinary medicinal preparations that were not used, or any leftover substances obtained upon use of a veterinary medicinal product, should be discarded as toxic waste; do not discard into wastewater.

13. FURTHER INFORMATION

Oclacitinib is a Janus kinase (JAK) inhibitor and can inhibit the function of cytokines dependent on JAK enzyme activity. The target cytokines of oclacitinib are those that are proinflammatory (which cause inflammation), or that are related to allergic responses or to pruritis. However, oclacitinib may affect other cytokines (for example, those involved in host (the dog) defense or hematopoiesis) and cause undesirable side effects.

• In addition to the active ingredient, the medicine also contains

Tablet core
Lactose monohydrate
Cellulose, microcrystalline
Sodium starch glycolate
Magnesium stearate

Tablet coating
Lactose monohydrate
Hypromellose (E464)
Titanium dioxide (E171)
Macrogol 400 (E1521)

• What the medicine looks like and the contents of the package

A white to off-white, oblong film-coated tablet with a score line on both sides, both sides are marked with the letters: AQ and S, M or L. The letters S, M or L refer to the different dosages of tablets: S refers to the 3.6 mg tablet, M to the 5.4 mg tablet, and L to the 16 mg tablet.

• Package sizes

An HDPE bottle of 100 pills with a child-proof cap.

• License Holder

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

• Manufacturer

Pfizer Italia S.R.L., Italy, Localita Marino del Tronto 63100, Ascoli Piceno, Italy
Or
Zoetis LLC (Subsidiary of Zoetis Inc.) USA, 2605 East Kilgore Road, Kalamazoo, Michigan 49001, USA.

- Revised in February 2021 according to MOH's guidelines.

• Registration number of the medicine in the National Drug Registry of the Ministry of Health

Apoquel 3.6 mg veterinary: 157-48-34524-00/01
Apoquel 5.4 mg veterinary: 157-49-34536-00/01
Apoquel 16 mg veterinary: 157-50-34535-00/01

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