

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg film-coated tablets for dogs
Apoquel 5.4 mg film-coated tablets for dogs
Apoquel 16 mg film-coated tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each film-coated tablet contains:

Apoquel 3.6 mg:	3.6 mg oclacitinib (as oclacitinib maleate)
Apoquel 5.4 mg:	5.4 mg oclacitinib (as oclacitinib maleate)
Apoquel 16 mg:	16 mg oclacitinib (as oclacitinib maleate)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

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.

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.

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.

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 naïve 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.

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, 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 $t_{1/2s}$ 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_{50s} 50-fold greater than the observed mean C_{max} (333 ng/ml or 0.997 μ M) 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Cellulose, microcrystalline
Lactose monohydrate
Magnesium stearate
Sodium starch glycolate

Tablet coating:

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

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.

Shelf life of the veterinary medicinal product as packaged for sale in bottles: 18 months.

Any remaining half tablets should be discarded after 3 days.

6.4 Special precautions for storage

Store below 25 °C.

Any remaining half tablet should be placed back in the opened blister and stored in the original cardboard carton, or in the HDPE bottle (for a maximum of 3 days).

6.5 Nature and composition of immediate packaging

All tablets strengths are packaged in either aluminium/PVC/Aclar or aluminium/PVC/PVDC blisters (each strip containing 10 film-coated tablets) packed into an outer cardboard box, or white HDPE plastic bottle with child resistant closure. Pack sizes of 20, 50 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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/154/001 (2 x 10 tablets, 3.6 mg)
EU/2/13/154/007 (5 x 10 tablets, 3.6 mg)
EU/2/13/154/002 (10 x 10 tablets, 3.6 mg)
EU/2/13/154/010 (20 tablets, 3.6 mg)
EU/2/13/154/011 (50 tablets, 3.6 mg)
EU/2/13/154/012 (100 tablets, 3.6 mg)
EU/2/13/154/003 (2 x 10 tablets, 5.4 mg)
EU/2/13/154/008 (5 x 10 tablets, 5.4 mg)
EU/2/13/154/004 (10 x 10 tablets, 5.4 mg)
EU/2/13/154/013 (20 tablets, 5.4 mg)
EU/2/13/154/014 (50 tablets, 5.4 mg)
EU/2/13/154/015 (100 tablets, 5.4 mg)
EU/2/13/154/005 (2 x 10 tablets, 16 mg)
EU/2/13/154/009 (5 x 10 tablets, 16 mg)
EU/2/13/154/006 (10 x 10 tablets, 16 mg)
EU/2/13/154/016 (20 tablets, 16 mg)
EU/2/13/154/017 (50 tablets, 16 mg)
EU/2/13/154/018 (100 tablets, 16 mg)
EU/2/13/154/019 (2 x 10 tablets, 3.6 mg)
EU/2/13/154/020 (5 x 10 tablets, 3.6 mg)
EU/2/13/154/021 (10 x 10 tablets, 3.6 mg)
EU/2/13/154/022 (2 x 10 tablets, 5.4 mg)
EU/2/13/154/023 (5 x 10 tablets, 5.4 mg)
EU/2/13/154/024 (10 x 10 tablets, 5.4 mg)
EU/2/13/154/025 (2 x 10 tablets, 16 mg)
EU/2/13/154/026 (5 x 10 tablets, 16 mg)
EU/2/13/154/027 (10 x 10 tablets, 16 mg)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12/09/2013.

Date of last renewal: 26/07/2018.

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg chewable tablets for dogs
Apoquel 5.4 mg chewable tablets for dogs
Apoquel 16 mg chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Apoquel 3.6 mg chewable tablets for dogs

Each chewable tablet contains 3.6 mg oclacitinib (as oclacitinib maleate).

Apoquel 5.4 mg chewable tablets for dogs

Each chewable tablet contains 5.4 mg oclacitinib (as oclacitinib maleate).

Apoquel 16 mg chewable tablets for dogs

Each chewable tablet contains 16 mg oclacitinib (as oclacitinib maleate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets.

Light to dark brown pentagon shaped mottled tablets with score lines on both sides. The tablets are debossed with the corresponding strength (“S S” for 3.6 mg, “M M” for 5.4 mg and “L L” for 16 mg).

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 IC₅₀s 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

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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/154/028-033

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12/09/2013.

Date of last renewal: 26/07/2018.

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

- A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. STATEMENT OF THE MRLs**

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Apoquel film-coated tablets

Name and address of the manufacturers responsible for batch release

Pfizer Italia S.R.L.
Via del Commercio 25/27
63100 Marino Del Tronto (AP)
ITALY

or

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

Apoquel chewable tablets

Name and address of the manufacturer responsible for batch release

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON for Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg film-coated tablets for dogs
Apoquel 5.4 mg film-coated tablets for dogs
Apoquel 16 mg film-coated tablets for dogs

oclacitinib

2. STATEMENT OF ACTIVE SUBSTANCES

3.6 mg oclacitinib per tablet (as oclacitinib maleate).
5.4 mg oclacitinib per tablet (as oclacitinib maleate).
16 mg oclacitinib per tablet (as oclacitinib maleate).

3. PHARMACEUTICAL FORM

Film-coated tablets

4. PACKAGE SIZE

20 tablets
50 tablets
100 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Store below 25 °C.

Any remaining half tablet should be stored in the blister and discarded if not used within 3 days.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/154/001 (2 x 10 tablets, 3.6 mg)
EU/2/13/154/007 (5 x 10 tablets, 3.6 mg)
EU/2/13/154/002 (10 x 10 tablets, 3.6 mg)
EU/2/13/154/003 (2 x 10 tablets, 5.4 mg)
EU/2/13/154/008 (5 x 10 tablets, 5.4 mg)
EU/2/13/154/004 (10 x 10 tablets, 5.4 mg)
EU/2/13/154/005 (2 x 10 tablets, 16 mg)
EU/2/13/154/009 (5 x 10 tablets, 16 mg)
EU/2/13/154/006 (10 x 10 tablets, 16 mg)
EU/2/13/154/019 (2 x 10 tablets, 3.6 mg)
EU/2/13/154/020 (5 x 10 tablets, 3.6 mg)
EU/2/13/154/021 (10 x 10 tablets, 3.6 mg)
EU/2/13/154/022 (2 x 10 tablets, 5.4 mg)
EU/2/13/154/023 (5 x 10 tablets, 5.4 mg)
EU/2/13/154/024 (10 x 10 tablets, 5.4 mg)
EU/2/13/154/025 (2 x 10 tablets, 16 mg)
EU/2/13/154/026 (5 x 10 tablets, 16 mg)
EU/2/13/154/027 (10 x 10 tablets, 16 mg)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON FOR BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg chewable tablets for dogs
Apoquel 5.4 mg chewable tablets for dogs
Apoquel 16 mg chewable tablets for dogs

oclacitinib

2. STATEMENT OF ACTIVE SUBSTANCES

3.6 mg oclacitinib per tablet (as oclacitinib maleate).
5.4 mg oclacitinib per tablet (as oclacitinib maleate).
16 mg oclacitinib per tablet (as oclacitinib maleate).

3. PHARMACEUTICAL FORM

Chewable tablet

4. PACKAGE SIZE

20 tablets
100 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP

11. SPECIAL STORAGE CONDITIONS

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.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/154/028 (2 x 10 chewable tablets, 3.6 mg)
EU/2/13/154/029 (10 x 10 chewable tablets, 3.6 mg)
EU/2/13/154/030 (2 x 10 chewable tablets, 5.4 mg)
EU/2/13/154/031 (10 x 10 chewable tablets, 5.4 mg)
EU/2/13/154/032 (2 x 10 chewable tablets, 16 mg)
EU/2/13/154/033 (10 x 10 chewable tablets, 16 mg)

17. MANUFACTURER'S BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

LABEL for Bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg film-coated tablets for dogs
Apoquel 5.4 mg film-coated tablets for dogs
Apoquel 16 mg film-coated tablets for dogs

oclacitinib

2. STATEMENT OF ACTIVE SUBSTANCES

3.6 mg oclacitinib per tablet (as oclacitinib maleate).
5.4 mg oclacitinib per tablet (as oclacitinib maleate).
16 mg oclacitinib per tablet (as oclacitinib maleate).

3. PHARMACEUTICAL FORM

Film-coated tablets

4. PACKAGE SIZE

20 tablets
50 tablets
100 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Store below 25 °C.

Any remaining half tablet should be stored in the bottle and discarded if not used within 3 days.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/154/010 (20 tablets, 3.6 mg)
EU/2/13/154/011 (50 tablets, 3.6 mg)
EU/2/13/154/012 (100 tablets, 3.6 mg)
EU/2/13/154/013 (20 tablets, 5.4 mg)
EU/2/13/154/014 (50 tablets, 5.4 mg)
EU/2/13/154/015 (100 tablets, 5.4 mg)
EU/2/13/154/016 (20 tablets, 16 mg)
EU/2/13/154/017 (50 tablets, 16 mg)
EU/2/13/154/018 (100 tablets, 16 mg)

17. MANUFACTURER’S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg tablets for dogs.

Apoquel 5.4 mg tablets for dogs.

Apoquel 16 mg tablets for dogs.

oclacitinib



2. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis

3. EXPIRY DATE

EXP {month/year}

4. BATCH NUMBER

Lot {number}

5. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg chewable tablets for dogs.
Apoquel 5.4 mg chewable tablets for dogs.
Apoquel 16 mg chewable tablets for dogs.

oclacitinib



2. NAME OF THE MARKETING AUTHORISATION HOLDER

Zoetis

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Apoquel 3.6 mg film-coated tablets for dogs
Apoquel 5.4 mg film-coated tablets for dogs
Apoquel 16 mg film-coated tablets for dogs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

Manufacturer responsible for batch release:

Pfizer Italia S.R.L.
Via del Commercio 25/27
63100 Marino Del Tronto (AP)
ITALY

or

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg film-coated tablets for dogs
Apoquel 5.4 mg film-coated tablets for dogs
Apoquel 16 mg film-coated tablets for dogs

oclacitinib

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each film-coated tablet contains 3.6 mg, 5.4 mg or 16 mg oclacitinib (as oclacitinib maleate).
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.

4. INDICATION(S)

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

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to oclacitinib 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.

6. ADVERSE REACTIONS

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%
Lack or loss of appetite (Anorexia)	2.6%	0%	1.4%	0%
New cutaneous or subcutaneous lumps	2.6%	2.7%	1.0%	0%
Weakness (Lethargy)	2.0%	1.4%	1.8%	1.4%
Excessive thirst (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.

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs



8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For oral use.

Dosage and treatment schedule:

The recommended initial dose of Apoquel tablets to be given to the dog is to achieve 0.4 to 0.6 mg oclacitinib/kg bodyweight, administered orally, twice daily for up to 14 days.

For maintenance therapy (after the initial 14 days of treatment), 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 by the responsible veterinarian.

These tablets can be administered with or without food.

Please see dosing table below for the number of tablets required to achieve the recommended dose. 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

9. ADVICE ON CORRECT ADMINISTRATION

Dogs should be carefully observed following administration to ensure that each tablet is swallowed.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store below 25 °C.

Any remaining half tablet should be placed back in the opened blister and stored in the original cardboard carton, or in the HDPE bottle (for a maximum of 3 days).

Do not use this veterinary medicinal product after the expiry date which is stated on the blister or bottle after EXP.

12. SPECIAL WARNING(S)

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 6), 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 label to the physician.

Pregnancy and lactation:

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.

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 naïve 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.

Overdose (symptoms, emergency procedures, 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu>).

15. OTHER INFORMATION

Apoquel tablets are supplied in either blister packs or bottles with 20, 50 or 100 tablets per pack. Not all pack sizes may be marketed.

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.

PACKAGE LEAFLET:
Apoquel 3.6 mg chewable tablets for dogs
Apoquel 5.4 mg chewable tablets for dogs
Apoquel 16 mg chewable tablets for dogs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apoquel 3.6 mg chewable tablets for dogs
Apoquel 5.4 mg chewable tablets for dogs
Apoquel 16 mg chewable tablets for dogs

oclacitinib

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each chewable tablet contains 3.6 mg, 5.4 mg or 16 mg oclacitinib (as oclacitinib maleate).

Light to dark brown pentagon shaped mottled tablets with score lines on both sides. The tablets are debossed with the corresponding strength (“S S” for 3.6 mg, “M M” for 5.4 mg and “L L” for 16 mg).

The tablets can be divided into equal halves.

4. INDICATION(S)

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

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to oclacitinib 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.

6. ADVERSE REACTIONS

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.

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs.



8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For oral use.

Dosage and treatment schedule:

The recommended initial dose of Apoquel tablets to be given to the dog is to achieve 0.4 to 0.6 mg oclacitinib/kg bodyweight, administered orally, twice daily for up to 14 days.

For maintenance therapy (after the initial 14 days of treatment), 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 by the responsible veterinarian.

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

These tablets can be administered with or without food.

Please see dosing table below for the number of tablets required to achieve the recommended dose. 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

9. ADVICE ON CORRECT ADMINISTRATION

Dogs should be carefully observed following administration to ensure that each tablet is swallowed.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister after EXP.

12. SPECIAL WARNING(S)

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 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.

Pregnancy and lactation:

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.

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.

Overdose (symptoms, emergency procedures, 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu>).

15. OTHER INFORMATION

Apoquel chewable tablets are supplied in blister packs with 20 or 100 tablets per pack. Not all pack sizes may be marketed.

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.