SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milprazon 4 mg/10 mg film-coated tablets for small cats and kittens weighing at least 0.5 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Active substances:
Milbemycin oxime 4 mg
Praziquantel 10 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Core:	
Cellulose, microcrystalline	
Lactose monohydrate	
Povidone	
Croscarmellose sodium	
Silica, colloidal anhydrous	
Magnesium stearate	
Coat:	
Hypromellose	
Talc	
Propylene glycol	
Titanium dioxide (E171)	0.51 mg
Meat Flavour	
Yeast powder	
Iron Oxide, yellow (E172)	0.20 mg

Brown yellow, oval, biconvex film-coated tablets with score line on one side.
The tablets can be divided into halves.

3. CLINICAL INFORMATION

3.1 Target species

Cats (small cats and kittens).

3.2 Indications for use for each target species

Treatment of mixed infections by immature and adult cestodes and nematodes of the following species:

- Cestodes:
Dipylidium caninum
Taenia spp.
Echinococcus multilocularis

- Nematodes:
Ancylostoma tubaeforme
Toxocara cati

Prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated.

3.3 Contraindications

Do not use in cats of less than 6 weeks of age and/or weighing less than 0.5 kg.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

It is recommended to treat all the animals living in the same household concomitantly.

In order to develop an effective worm control programme local epidemiological information and the risk of exposure of the cat should be taken into account, and it is recommended to seek professional advice.

When *D. caninum* infection is present, concomitant treatment against intermediate hosts, such as fleas and lice, should be considered to prevent re-infection.

Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class.

3.5 Special precautions for use

Special precautions for safe use in the target species:

No studies have been performed with severely debilitated cats or individuals with seriously compromised kidney or liver function. The veterinary medicinal product is

not recommended for such animals or only according to a benefit/risk assessment by the responsible veterinarian.
Ensure cats and kittens weighing between 0.5 kg and ≤2 kg receive the appropriate tablet strength (4 mg milbemycin oxime/10 mg praziquantel) and the appropriate dose (1/2 or 1 tablet) for the corresponding weight band (1/2 tablet for cats weighing 0.5 to 1 kg; 1 tablet for cats weighing >1 to 2 kg).
As the tablets are flavoured, they should be stored in a safe place out of the reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

People with known hypersensitivity to the active substances or the excipients should avoid contact with the veterinary medicinal product.
In the event of accidental ingestion of the tablets, particularly by a child, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.
Part tablets should be returned to the open blister pocket and inserted into the outer carton.

Special precautions for the protection of the environment:

Not applicable.

Other precautions:

Echinococcosis represents a hazard for humans. As Echinococcosis is a notifiable disease to the World Organisation for Animal Health (WOAH), specific guidelines on the treatment and follow-up, and on the safeguard of persons, need to be obtained from the relevant competent authority.

3.6 Adverse events

Cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction; Systemic disorder (e.g. lethargy)*; Neurological disorder (e.g. muscle tremors and ataxia)*; Digestive tract disorder (e.g. emesis and diarrhoea)*.

*Especially in young cats.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Fertility:

Can be used in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

No interactions were observed when the recommended dose of the macrocyclic lactone selamectin was administered during treatment with milbemycin oxime and praziquantel at the recommended dose.
Although not recommended, the concomitant use of milbemycin oxime and praziquantel with a spot-on containing moxidectin and imidacloprid at recommended dose rates following a single application was well tolerated in one laboratory study in 10 kittens.
The safety and efficacy of the concurrent use have not been investigated in field studies.
In the absence of further studies, caution should be taken in the case of concurrent use of the veterinary medicinal product and other macrocyclic lactones. Also, no such studies have been performed with reproducing animals.

3.9 Administration routes and dosage

Oral use.
To ensure a correct dosage, body weight should be determined as accurately as possible.

Minimum recommended dose rate: 2 mg of milbemycin oxime and 5 mg of praziquantel per kg are given orally as a single dose. The veterinary medicinal product should be administered with or after some food. Doing so ensures optimum protection against heartworm disease.
Depending on the bodyweight of the cat, the practical dosing is as follows:

Body weight	**Film-coated tablets for small cats and kittens**
0.5 - 1 kg	½ tablet
> 1 - 2 kg	1 tablet

The veterinary medicinal product can be inserted into a programme for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. For the prevention of heartworm disease: the veterinary medicinal product kills *Dirofilaria immitis* larvae up to one month after their transmission by mosquitoes. For regular prevention of heartworm disease the use of a monosubstance is preferred.

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

In case of overdose, in addition to signs observed at the recommended dose (see 3.6), drooling may be observed. This sign will usually disappear spontaneously within a day.

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:

QP54AB51

4.2 Pharmacodynamics

Milbemycin oxime belongs to the group of macrocyclic lactones, isolated from the fermentation of *Streptomyces hygroscopicus* var. *aureolacrimosus*. It is active against mites, against larval and adult stages of nematodes as well as against larvae of *Dirofilaria immitis*.

The activity of milbemycin is related to its action on invertebrate neurotransmission: Milbemycin oxime, like avermectins and other milbemycins, increases nematode and insect membrane permeability to chloride ions via glutamate-gated chloride ion channels (related to vertebrate $GABA_A$ and glycine receptors). This leads to hyperpolarisation of the neuromuscular membrane and flaccid paralysis and death of the parasite.

Praziquantel is an acylated pyrazino-isoquinoline derivative. Praziquantel is active against cestodes and trematodes. It modifies the permeability for calcium (influx of Ca^{2+}) in the membranes of the parasite inducing an imbalance in the membrane structures, leading to membrane depolarisation and almost instantaneous contraction of the musculature (tetany), rapid vacuolisation of the syncytial tegument and subsequent tegumental disintegration (blebbing), resulting in easier expulsion from the gastrointestinal tract or death of the parasite.

4.3 Pharmacokinetics

In cats under fed condition, praziquantel reaches peak plasma concentrations within 3 hours after oral administration.
The half life of elimination is around 2 hours.

After oral administration in cats under fed condition, milbemycin oxime reaches peak plasma concentrations within 5 hours. The half life of elimination is around 43 hours (± 21 hours).
In the rat, metabolism appears to be complete although slow, since unchanged milbemycin oxime has not been found in urine or feces. Main metabolites in the rat are monohydroxylated derivatives, attributable to hepatic biotransformation. In addition to relatively high liver concentrations, there is some concentration in fat, reflecting its lipophilicity.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life for halved tablets after first opening the immediate packaging: 6 months.

5.3 Special precautions for storage

Store in the original package in order to protect from moisture.
Halved tablets should be stored below 25°C in the original blister and be used for the next administration.
Keep the blister in the outer carton.

5.4 Nature and composition of immediate packaging

Blister packs consisting of cold formed OPA/Al/PVC foil and aluminium foil.
Box with 1 blister of 2 tablets.
Box with 1 blister of 4 tablets.
Box with 12 blisters, each blister contains 4 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

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

The veterinary medicinal product should not enter water courses as milbemycin oxime may be dangerous for fish and other aquatic organisms.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto

7. MARKETING AUTHORISATION NUMBER

Vm 01656/3077

8. DATE OF FIRST AUTHORISATION

11 May 2015

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

April 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription (BG, CY, GR, HU, PL, CZ, DE, EE, ES, HR, IE, IT, LV, PT, RO, SI, SK, UK (NI)).
Veterinary medicinal product not subject to prescription (BE, NL, LT).
Veterinary medicinal product subject to prescription except for some pack sizes (FR, SE).

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

Gavin Hall
Approved: 06 July 2024