Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbactor 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:

Iron Oxide, yellow (E172)	0.20 mg
Titanium dioxide (E171)	0.51 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

4 CLINICAL PARTICULARS

4.1 Target Species

Cats (small cats and kittens).

4.2 Indications for use, specifying the target species

In cats: 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.

4.3 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 known cases of hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings for each target species

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.

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.

4.5 Special precautions for use

Special precautions for use in animals
No studies have been performed with severely debilitated cats or individuals with seriously compromised kidney or liver function. The 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).

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 doctor.
Wash hands after use.

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

4.6 Adverse reactions (frequency and seriousness)

On very rare occasions, especially in young cats, systemic signs (such as lethargy), neurological signs (such as ataxia and muscle tremors) and/or gastrointestinal signs (such as emesis and diarrhoea) have been observed after administration of the combination milbemycin/praziquantel.
On very rare occasions hypersensitivity reactions have been observed following administration of the product.

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 veterinary medicinal product can be used in breeding cats including pregnant and lactating queens.

4.8 Interaction with other medicinal products and other forms of interactions

The concurrent use of the milbemycin oxime and praziquantel with selamectin is well tolerated. 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. In the absence of further studies, caution should be taken in the case of concurrent use of the product and other macrocyclic lactones. Also, no such studies have been performed with reproducing animals.

4.9 Amounts to be administered and administration route

Oral use.
Animals should be weighed to ensure accurate dosing.
Minimum recommended dose rate: 2 mg of milbemycin oxime and 5 mg of praziquantel per kg are given orally as a single dose. The 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:

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

The product can be inserted into a programme for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. The product has a duration of heartworm prevention of one month. For regular prevention of heartworm disease the use of a monosubstance is preferred.

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

In case of overdose, in addition to signs observed at the recommended dose (see 4.6), drooling may be observed. This sign will usually disappear spontaneously within a day.

4.11 Withdrawal period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents: endectocides; milbemycin, combinations
ATCvet code: QP54AB51

5.1 Pharmacodynamic properties

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 vacuolization of the syncytial tegument and subsequent tegumental disintegration (blebbing), resulting in easier expulsion from the gastrointestinal tract or death of the parasite.

5.2 Pharmacokinetic particulars

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Cellulose, microcrystalline
Lactose monohydrate
Povidone
Croscarmellose sodium
Silica, colloidal anhydrous
Magnesium stearate

Coat:
Hypromellose
Talc
Propylene glycol
Titanium dioxide (E171)
Meat Flavour
Yeast powder
Iron Oxide, yellow (E172)

6.2 Major incompatibilities

Not applicable.

6.3 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: 3 months.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.
This veterinary medicinal product does not require any special temperature storage conditions.
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.

6.5 Nature and composition of immediate packaging

Blister packs consisting of cold formed OPA/Al/PVC foil and aluminium foil.
Box with 1 blister of 4 tablets.
Box with 12 blisters, each blister contains 4 tablets.
Not all pack sizes may be marketed.

6.6 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 derived from such veterinary medicinal product should be disposed of in accordance with local requirements.
The product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

7 MARKETING AUTHORISATION HOLDER

Krka, d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8 MARKETING AUTHORISATION NUMBER(S)

VPA10774/032/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 July 2015
Date of last renewal: 08 May 2020

10 DATE OF REVISION OF THE TEXT

June 2021