# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milpro 12.5 mg/125 mg film-coated tablets for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
**Active substances:**
Milbemycin oxime 12.5 mg
Praziquantel 125 mg

**Excipients:**
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Film-coated tablet.
Round shaped, beige to pale brown meat flavoured tablets.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs

### 4.2 Indications for use, specifying the target species

In dogs: treatment of mixed infections by adult cestodes (tapeworms) and nematodes (roundworms) of the following species:
Cestodes:
*Dipylidium caninum*
*Taenia* spp.,
*Echinococcus* spp.,
*Mesocestoides* spp.
Nematodes:
*Ancylostoma caninum,*
*Toxocara canis,*
*Toxascaris leonina,*
*Trichuris vulpis,*
*Thelazia callipaeda* (see specific treatment schedules under section 4.9 “Amounts to be administered and administration route”),
*Crenosoma vulpis* (Reduction of the level of infection),
*Angiostrongylus vasorum* (Reduction of the level of infection by immature adult (L5) and adult parasite stages; see specific treatment and disease prevention schedules under section “4.9 Amounts to be administered and administration route”).

The product can also be used in the prevention of heartworm disease (*Dirofilaria immitis*), if concomitant treatment against cestodes is indicated.

## 4.3 Contraindications

Do not use in dogs weighing less than 5 kg

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
See also point "Special precautions for use".

## 4.4 Special warnings for each target species

In order to develop an effective worm control programme local epidemiological information and the living conditions of the dog should be taken into account and therefore it is recommended to seek professional advice.

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

It is recommended to treat all the animals in the same household concomitantly.
When *Dipylidium caninum* infection is present, concomitant treatment against intermediate hosts, such as fleas and lice, should be considered to prevent re-infection

## 4.5 Special precautions for use

4.5 i Special precautions for use in animals

Studies with milbemycin oxime indicate that the margin of safety in certain dogs of Collie or related breeds is less than in other breeds. In these dogs, the recommended dose should be strictly observed.
The tolerance of the product in young puppies from these breeds has not been investigated.
Clinical signs in Collies are similar to those seen in the general dog population when overdosed (see also section 4.10).

As per good veterinary practice, animals should be weighed to ensure accurate dosing.

Treatment of dogs with a high number of circulating microfilariae can sometimes lead to the appearance of hypersensitivity reactions, such as pale mucous membranes, vomiting, trembling, laboured breathing or excessive salivation. These reactions are associated with the release of proteins from dead or dying microfilariae and are not a direct toxic effect of the product. The use in dogs suffering from microfilaremia is thus not recommended.

In heartworm risk-areas, or in the case it is known that a dog has been travelling to and from heartworm risk regions, before using the product, a veterinary consultation is advised to exclude the presence of any concurrent infestation of *Dirofilaria immitis*. In the case of a positive diagnosis, adulticidal therapy is indicated before administering the product.

No studies have been performed with severely debilitated dogs 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.

In dogs less than 4 weeks old, tapeworm infection is unusual. Treatment of animals less than 4 weeks old with a combination product may therefore not be necessary.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

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

Wash hands after use.
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.
Do not handle this product in case of known hypersensitivity to the active substances or to any of the excipients.

4.5 iii 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)

Hypersensitivity reactions, systemic signs (such as lethargy), neurological signs (such as muscle tremors, ataxia and convulsions) and/or gastrointestinal signs (such as emesis, diarrhoea, anorexia and drooling) may be observed, in very rare occasions, in dogs after administration of the veterinary medicinal 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

In a study, this combination of active substances was demonstrated to be well tolerated in breeding bitches, including during pregnancy and lactation. As a specific study with this product has not been performed, use during pregnancy and lactation only according to a benefit/risk assessment by the responsible veterinarian.

## 4.8 Interaction with other medicinal products and other forms of interaction

The concurrent use of the combination praziquantel/milbemycin oxime with selamectin is well tolerated. No interactions were observed when the recommended dose of the macrocyclic lactone selamectin was administered during treatment with the combination 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.
Minimum recommended dose rate: 0.5 mg of milbemycin oxime and 5 mg of praziquantel per kg are given once orally.

The product should be administered with or after some food.
The tablets are meat flavoured and easy to administer (usually dogs and puppies will accept them voluntarily even without any food).

Depending on the bodyweight of the dog, the practical dosing is as follows:

| Weight | Tablets |
|---|---|
| 5 – 25 kg | 1 tablet |
| >25 – 50 kg | 2 tablets |
| >50 – 75 kg | 3 tablets |

In cases when heartworm disease prevention is used and at the same time treatment against tapeworm is required, the product can replace the monovalent product for the prevention of heartworm disease.

For treatment of *Angiostrongylus vasorum* infections, milbemycin oxime should be given four times at weekly intervals. It is recommended, where concomitant treatment against cestodes is indicated, to treat once with the product and continue with the monovalent product containing milbemycin oxime alone, for the remaining three weekly treatments.
In endemic areas administration of the product every four weeks will prevent angiostrongylosis by reducing immature adult (L5) and adult parasite burden, where concomitant treatment against cestodes is indicated.

For the treatment of *Thelazia callipaeda*, milbemycin oxime should be given in 2 treatments, seven days apart. Where concomitant treatment against cestodes is indicated, the product can replace the monovalent product containing milbemycin oxime alone.

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

No other signs than those observed at the recommended dose have been observed (see section 4.6 “Adverse reactions (frequency and seriousness)”).

## 4.11 Withdrawal period(s)

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

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

### 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 Ca2+) 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

After oral administration of praziquantel in the dog, peak serum levels of parent are rapidly attained (Tmax approximately 0.5-4 hours) and decline quickly ($t_{1/2}$ approximately 1.5 hours); there is a substantial hepatic first-pass effect, with very rapid and almost complete hepatic biotransformation, principally to monohydroxylated (also some di- and tri-hydroxylated) derivatives, which are mostly glucuronide and/or sulfate conjugated before excretion. Plasma binding is about 80%. Excretion is fast and complete (about 90% in 2 days); the principal route of elimination is renal.

After oral administration of milbemycin oxime in dogs, peak plasma levels occur at about 2-4 hours, and decline with a half-life of the unmetabolised milbemycin oxime of 1-4 days. Bioavailability is about 80%.
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:
Microcrystalline cellulose
Croscarmellose sodium
Lactose monohydrate
Starch, pregelatinised
Povidone
Magnesium stearate
Silica hydrophobic colloidal

Coat:
Natural Poultry liver flavour
Hypromellose
Microcrystalline cellulose
Macrogol stearate

### 6.2 Major incompatibilities

Not applicable.

### 6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

### 6.4 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
Keep the blister in the outer carton.

### 6.5 Nature and composition of immediate packaging

Aluminium/ Aluminium blister pack (Oriented polyamide/Aluminium/Polyvinyl chloride sealed to Aluminium film).

Available pack sizes:
Cardboard box of 2 tablets containing 1 blister of 2 tablets
Cardboard box of 4 tablets containing 2 blisters of 2 tablets
Cardboard box of 24 tablets containing 12 blisters of 2 tablets
Cardboard box of 48 tablets containing 24 blisters of 2 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 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

VIRBAC
1ère avenue – 2065m – LID
06516 Carros
FRANCE

## 8. MARKETING AUTHORISATION NUMBER

Vm 05653/4182

## 9. DATE OF FIRST AUTHORISATION

15 July 2014

## 10. DATE OF REVISION OF THE TEXT

September 2021

Approved: 23/09/21