

# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

MILBEMAX® tablets for dogs

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains:

### Active substances:

Milbemycin oxime	12.5 mg
Praziquantel	125.0 mg

For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Tablet

Round shaped, white. One side bears the imprint "CCA", the other side "NA".

## 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 and nematodes of the following species susceptible to praziquantel and milbemycin oxime:

- Cestodes:

*Dipylidium caninum*

*Taenia spp.*

*Echinococcus spp.*

*Mesocestoides spp.*

- Nematodes:

*Ancylostoma caninum*

*Toxocara canis*

*Toxascaris leonine*

*Trichuris vulpis*

*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 SPC point 4.9 "Amounts to be administered and administration route")

*Thelazia callipaeda* (see specific treatment schedule 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 case of hypersensitivity to the active substances or to any of the excipients.

See also section 4.5 "Special precautions for use".

### **4.4 Special warnings for each target species**

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

When infection with the cestode *D. caninum* has been confirmed, concomitant treatment against intermediate hosts, such as fleas and lice, should be discussed with a veterinarian to prevent re-infection.

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 MILBEMAX 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 section 4.10).

### **4.5 Special precautions for use**

#### Special precautions for use in animals

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 MILBEMAX, 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 MILBEMAX.

Echinococcosis represents a hazard for humans. In case of Echinococcosis, specific guidelines on the treatment and follow up and on the safeguard of persons have to be followed. Experts or institutes of parasitology should be consulted.

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

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

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

Wash hands after use.

In case 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.

#### **4.6 Adverse reactions (frequency and seriousness)**

In very rare occasions, hypersensitivity reactions, systemic signs (such as lethargy), neurological signs (such as muscle tremors and ataxia) and/or gastrointestinal signs (such as emesis, diarrhoea, anorexia and drooling) have been observed 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

The product may be used in breeding dogs including pregnant and lactating bitches.

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

The concurrent use of MILBEMAX with selamectin is well tolerated. No interactions were observed when the recommended dose of the macrocyclic lactone selamectin was administered during treatment with MILBEMAX at the recommended dose. In the absence of further studies, caution should be taken in the case of concurrent use of MILBEMAX and other macrocyclic lactones. Also no such studies have been performed with reproducing animals.

#### 4.9 Amounts to be administered and administration route

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.

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, MILBEMAX 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 MILBEMAX 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, MILBEMAX 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).

#### **4.11 Withdrawal period(s)**

Not applicable

### **5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES**

Pharmacotherapeutic group: Endectocides

ATCvet Code : QP54A B51 (milbemycin oxime, 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<sub>A</sub> 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<sup>2+</sup>) 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 ( $T_{max}$  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 milbemyacin oxime in dogs, peak plasma levels occur at about 2-4 hours, and decline with a half-life of the unmetabolised milbemyacin oxime of 1-4 days. Bioavailability is about 80%.

In the rat, metabolism appears to be complete although slow, since unchanged milbemyacin 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**

Cellulose, microcrystalline  
Croscarmellose sodium  
Povidone  
Lactose monohydrate  
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: 2 years

### **6.4 Special precautions for storage**

Do not store above 30 °C  
Keep the blister in the outer carton in order to protect from light

### **6.5 Nature and composition of immediate packaging**

PVC/PE/PVdC/aluminium blister  
Available package sizes:  
Box with 2 tablets in blister  
Box with 4 tablets in blister  
Box with 10 tablets in blister  
Box with 20 tablets in blister

Box with 50 tablets in blister  
Box with 100 tablets in blister

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.

MILBEMAX should not enter water courses as this may be dangerous for fish and other aquatic organisms.

### **7 MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Strasse 4  
27472 Cuxhaven  
Germany

### **8 MARKETING AUTHORISATION NUMBER(S)**

VPA22020/008/002

### **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 8<sup>th</sup> August 2003  
Date of last renewal: 1<sup>st</sup> August 2007

### **10 DATE OF REVISION OF THE TEXT**

October 2018