Milbemax chewable tablets for dogs

Species: Dogs

Therapeutic indication: **Pharmaceuticals: Endoparasiticides:** Anthelmintics for dogs

Active ingredient: Milbemycin Oxime, Praziquantel

Product: Milbemax® chewable tablets for dogs

Product index: Milbemax chewable tablets for dogs

Qualitative and quantitative composition

One chewable tablet contains:

Active substances:

Milbemycin oxime 12.5 mg

Praziquantel 125.0 mg

Excipients:

Glycerol (E422) 460.46 mg

Propylene glycol (E 1520) 4.54 mg

Iron oxide, brown (E 172) 3.29 mg

Butylhydroxyanisole (E 320) 1.32 mg

Propyl gallate (E 310) 0.46 mg

For the full list of excipients, see Pharmaceutical Particulars.

Pharmaceutical form

Chewable tablet Oval shaped, dark brown

Clinical particulars

Target species

Dogs

Indications for use, specifying the target species

In dogs : treatment of mixed infections by adult cestodes and nematodes of the following species:

- Cestodes:

Dipylidium caninum

Taenia spp.

Echinococcus spp.

Mesocestoides spp.

- Nematodes:

Ancylostoma caninum

Toxocara canis

Toxascaris leonina

Trichuris vulpis

Crenosoma vulpis

Angiostrongylus vasorum (Reduction of the level of infection by immature adult (L5) and adult parasite stages) (see “Amounts to be administered and administration route”)

Thelazia callipaeda (see “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.

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 excipients.

See also section "Special precautions for use".

Special warnings for each target species

None.

Special precautions for use

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 “Overdose” section).

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, 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.

People with known hypersensivity to any of the ingredients should avoid contact with the veterinary medicinal product.

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 doctor.

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.

Adverse reactions (frequency and seriousness)

In very rare occasions, systemic signs (such as lethargy), neurological signs (such as muscle tremors, ataxia and convulsions) and/or gastrointestinal signs (such as emesis, drooling, diarrhoea and anorexia) have been observed in dogs after administration of the veterinary medicinal product.

The frequency of possible adverse effects is defined using the following convention:

very common (affects more than 1 animal in 10)

common (affects 1 to 10 animals in 100)

uncommon (affects 1 to 10 animals in 1,000)

rare (affects 1 to 10 animals in 10,000)

very rare (affects less than 1 animals in 10,000)

not known (frequency cannot be estimated from the available data)

Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has been established during pregnancy and lactation.

Can be used in pregnant and lactating bitches.

Can be used in breeding animals.

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 the product at the recommended dose.

Although not recommended, the concomitant use of the product with a spot on containing moxidectin and imidacloprid at recommended dose rates following a single application was well tolerated in one experimental study by beagle dogs at the age 11 months or older. Transient neurological adverse reactions (poor proprioception, flaccid frontal and hind legs, incoordination, slight tremors and high stepping gait of the hind limbs only) were observed after administration of both products or of the spot-on only in another study conducted in puppies aged 8-12 weeks.

The safety and efficacy of this combination have not been investigated in field studies.

In the absence of further studies, caution should be taken in the case of concurrent use of MILBEMAX and any other macrocyclic lactone. Also, no such studies have

been performed with reproducing animals, Collies, related breeds and their crosses.

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	**Number of Tablet**
5 – 25 kg	1 tablet
> 25 - 50 kg	2 tablets
> 50 - 75 kg	3 tablets

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid under dosing.

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*, milbemcyin 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.

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

The adverse reactions observed are the same as those observed at the recommended dose (see “Adverse reactions” section) but more pronounced.

Withdrawal period(s)

Not applicable.

Pharmacological particulars

Pharmacotherapeutic group: Endectocides

ATCvet Code : QP54A B51 (milbemycin oxime, combinations)

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.

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 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 faeces. 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.

Pharmaceutical particulars

List of excipients

Glycerol (E422)

Propylene glycol (E 1520)

Iron oxide, brown (E 172)

Butylhydroxyanisole (E 320)

Propyl gallate (E 310)

Starch, pregelatinised

Natural chicken flavour

Confectioner’s sugar NF

Water, purified

Sodium chloride

Citric acid monohydrate

Incompatibilities

Not applicable.

Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.

Special precautions for storage

Do not store above 25 °C.

Nature and composition of immediate packaging

Aluminum/aluminum blister (OPA/Al/PVC//Al/Heat-Seal coating) or aluminum strip (polyester/Al/PE)

Available pack sizes:

1 box with 1 blister of 2 chewable tablets

1 box with 1 blister of 4 chewable tablets

1 box with 12 blisters, each blister contains 4 chewable tablets

1 box with 24 blisters, each blister contains 4 chewable tablets

1 box with 1 strip of 2 chewable tablets

1 box with 1 strip of 4 chewable tablets

1 box with 12 strips, each strip contains 4 chewable tablets

Not all pack sizes may be marketed.

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

Marketing Authorisation Number

Vm 00879/4043

Date of the first authorisation or date of renewal

08 January 2010

Date of revision of the text

March 2016

Legal category

Legal category:POM-V

GTIN

GTIN description:MILBEMAX CHEWY 12.5/125MG TAB 4 PK ST

GTIN:05037694053246

GTIN description:MILBEMAX CHEWY 12.5/125MG TAB 4 X 12 ST

GTIN:05037694053222