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Milprazon CHEWABLE Tablets for Dogs

Species: Dogs

Active ingredient: Milbemycin Oxime, Praziquantel

Product: Milprazon Chewable 2.5 mg/25 mg Film-coated Tablets for Small Dogs and Puppies Weighing at Least 0.5 kg

Product index: Milprazon CHEWABLE

Incorporating: Milprazon Chewable 12.5 mg/125 mg Film-coated Tablets for Dogs Weighing at Least 5 kg

Presentation

Milprazon CHEWABLE 2.5 mg/25 mg film-coated Tablets for Small Dogs and Puppies weighing at least 0.5kg. Film-coated tablet. Pale yellowish brown, oval, biconvex, mottled, film-coated tablets, scored on one side. The tablets can be divided into equal halves.

Milprazon CHEWABLE 12.5 mg/125 mg film-coated Tablets for Dogs weighing at least 5 kg. Tablet. Yellowish-white with brown spots, round, slightly biconvex tablets.

	Milbemycin Oxime
Milprazon CHEWABLE Tablets for Small Dogs and Puppies	2.5
Milprazon CHEWABLE Tablets for Dogs	12.5

Uses

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* (Reduction of the level of infection); *Angiostrongylus vasorum*, (Reduction of the level of infection by immature adult (L5) and adult parasite stages), *Thelazia callipaeda*.

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

Dosage and administration

FOR ORAL USE;

Animals should be weighed to ensure accurate dosing.

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 food.

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

Body Weight	Film-coated tablets
5 - 25 kg	1 tablet
>25 - 50 kg	2 tablet
>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.

Use during pregnancy and lactation: The product may be used in breeding dogs including pregnant and lactating bitches.

Contra-indications, warnings, etc

Contraindications

Milprazon CHEWABLE 2.5 mg/25 mg film-coated Tablets for Small Dogs and Puppies Weighing At Least 0.5 kg. Do not use in puppies of less than 2 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.

Milprazon CHEWABLE 12.5 mg/125 mg film-coated Tablets for Dogs Weighing At Least 5 kg. 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.

Special warnings for use in animals: Special warnings for each target species 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. In order to develop an effective worm control programe local epidemiological information and the risk of exposure of the dog 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.

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. 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 veterinary medicinal product. No studies have been performed with severely debilitated dogs 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.

In dogs less than 4 weeks old, tape worm infection is unusual. Treatment of animals less than 4 weeks old with a combination veterinary medicinal product may therefore not be necessary. As the tablets are flavoured, they should be stored in a safe place out of the reach of animals.

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.

User safety: Accidental ingestion of a tablet by a child may be harmful. In order to prevent children from accessing the product, tablets should be administered and stored out of sight and reach of

children. Wash hands after use. Part tablets should be returned to the open blister pocket and inserted into the outer carton. 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.

Adverse reactions: On very rare occasions, hypersensitivity reaction, systemic disorders (such as lethargy), neurological disorders (such as muscle tremors and ataxia) and/or digestive tract disorders (such as emesis, diarrhoea, anorexia and drooling) have been observed in dogs after administration of the combination of milbemycin oxime and praziquantel.

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 contact details.

Overdose: No other signs than those observed at the recommended dose have been observed

Interactions 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 combination of 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.

Major incompatiblities: Not applicable

Pharmaceutical precautions

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

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.

Legal category

Legal category:POM-V

Packaging quantities

Blister packs consisting of cold formed OPA/Al/PVC foil and aluminium foil.

Cardboard box with 1 blister of 2 tablets.

Cardboard box with 1 blister of 4 tablets.

Cardboard box with 12 blisters, each blister contains 4 tablets (total 48 tablets).

Not all pack sizes may be marketed.

Marketing Authorisation Holder (if different from distributor)

KRKA, d.d., Novo mesto

Šmarješka cesta 6

8501 Novo mesto

Slovenia

Further information

Pharmacotherapeutic group: Endectocides, Macrocyclic lactones, milbemycin, combinations.

ATCvet code: QP54AB51

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 GABAA 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.

Pharmacokinectic particulars

After oral administration of praziquantel in the dog, after a small amount of food, peak serum levels of parent are rapidly attained (Tmax approximately 0.25-2.5 hours) and decline quickly (t1/2 approximately 1 hour); 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, after a small amount of food, peak plasma levels occur at about 0.75-3.5 hours, and decline with a half-life of the unmetabolised milbemycin oxime of 1-4 days. Bioavailability is about 80%.

Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater. The veterinary medicinal product should not enter water courses as milbemycin oxime may be dangerous for fish and other aquatic organisms. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

List of excipients

Cellulose microcrystalline, Lactose monohydrate, Povidone, Croscarmellose sodium, Silica colloidal anhydrous, Meat Flavour, Yeast, Magnesium stearate, Hypromellose, Talc, Propylene Glycol, Liver Flavour

Marketing Authorisation Number

Milprazon CHEWABLE Tablets for Small Dogs and Puppies: Vm 01656/5082

Milprazon CHEWABLE Tablets for Dogs: Vm 01656/5083

Significant changes

GTIN

GTIN description:MILPRAZON CHEWABLE FCT 12,5/125MG 4 GB

GTIN:3838989741662 (KOS)

GTIN description:MILPRAZON CHEWABLE FCT 12,5/125MG 48 GB

GTIN:3838989741693 (KOS)

GTIN description:MILPRAZON CHEWABLE FCT 2,5/25MG 48 GB

GTIN:3838989741686 (KOS)