

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbetab 12.5 mg/125 mg Flavoured Tablets for Dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

### 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

A brown flat round shaped tablet with a break line on one side.

## 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:

- 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; 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 2.5 kg

Do not use in case 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**

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 Milbetab Flavoured Tablets for Dogs 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 in point 4.10).

#### **4.5 Special precautions for use, including special precautions to be taken by the person administering the medicinal product to animals**

##### **i. 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 Milbetab Flavoured Tablets for Dogs, 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 Milbetab Flavoured Tablets for Dogs.

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

##### **ii. Special precautions to be taken by the person administering the veterinary medicinal product to animals**

Wash hands after use.

Keep out of sight and reach of children.

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.

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

In very rare occasions, 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 interaction**

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

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

In cases when heartworm disease prevention is used and at the same time treatment against tapeworm is required, Milbetab Flavoured Tablets for Dogs 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 Milbetab Flavoured Tablets for Dogs 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, Milbetab Flavoured Tablets for Dogs 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 4.6)

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

Not applicable

### **5. PHARMACOLOGICAL PROPERTIES**

**Pharmacotherapeutic group:** Endectocides

**ATCvet Code:** QP54A B51 (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<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 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

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Cellulose, microcrystalline  
Croscarmellose sodium  
Povidone K30  
Lactose monohydrate  
Silica, colloidal anhydrous  
Magnesium stearate  
Talc  
Artificial Powdered Beef Flavour  
Yeast Extract

### **6.2 Major incompatibilities**

Not applicable.

### **6.3 Shelf life**

Shelf-life of the veterinary medicinal product as packaged for sale: 18 months

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

Do not store above 25°C.

Keep blister in the outer carton to protect from light.

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

Blister consisting of clear PVC/PE/PVDC film and an aluminium foil.

Box with 2, 4 10, 20, 30, 50 or 100 tablets in blisters.

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 come into contact with water courses as this may be dangerous for fish and other aquatic organisms.

### **7. MARKETING AUTHORISATION HOLDER**

Chanelle Pharmaceuticals Manufacturing Limited,  
Loughrea.  
Co. Galway,  
Ireland.

### **8. MARKETING AUTHORISATION NUMBER**

### **9. DATE OF FIRST AUTHORISATION**

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

### **ANNEX III**

### **LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON <THE OUTER PACKAGE> <AND> <THE IMMEDIATE PACKAGE>**

**{NATURE/TYPE}**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Milbetab 12.5 mg/125 mg Flavoured Tablets for Dogs

**2. STATEMENT OF ACTIVE SUBSTANCES**

Milbemycin oxime	12.5 mg
Praziquantel	125.0 mg

**3. PHARMACEUTICAL FORM**

Tablet

**4. PACKAGE SIZE**

2, 4 10, 20, 30, 50 or 100

**5. TARGET SPECIES**

Dogs

**6. INDICATION(S)**

In dogs: treatment of mixed infections by gastrointestinal roundworms, tapeworms, hookworms and whipworms and also for the treatment and prevention of the lungworm *Angiostroglyus vasorum* and prevention of the heartworm *Dirofilaria immitis*, where concomitant tapeworm treatment is indicated.

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use only.  
Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

N/A

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C.

Keep blister in the outer carton to protect from light.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Read the package leaflet before use.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only.

**14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”**

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Chanelle Pharmaceuticals Manufacturing Ltd.  
Dublin Road  
Loughrea  
Co. Galway  
Ireland

**16. MARKETING AUTHORISATION NUMBER(S)**

**17. MANUFACTURER’S BATCH NUMBER**

<b>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</b>
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{NATURE/TYPE}
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<b>1. NAME OF THE VETERINARY MEDICINAL PRODUCT</b>
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Milbetab 12.5 mg/125 mg Flavoured Tablets for Dogs

<b>2. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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Chanelle

<b>3. EXPIRY DATE</b>
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<b>4. BATCH NUMBER</b>
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<b>5. THE WORDS “FOR ANIMAL TREATMENT ONLY”</b>
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For animal treatment only.

**B. PACKAGE LEAFLET**

## **PACKAGE LEAFLET:**

### **Milbetab 12.5 mg/125 mg Flavoured Tablets for Dogs**

#### **1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Chanelle Pharmaceuticals Manufacturing Ltd.  
Dublin Road  
Loughrea  
Co. Galway  
Ireland

#### **2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Milbetab 12.5 mg/125 mg Flavoured Tablets for Dogs

#### **3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)**

Milbemycin oxime	12.5 mg
Praziquantel	125.0 mg

#### **4. INDICATION(S)**

In dogs: treatment of mixed infections by gastrointestinal roundworms, tapeworms, hookworms and whipworms and also for the treatment and prevention of the lungworm *Angiostrongylus vasorum* and prevention of the heartworm *Dirofilaria immitis*, where concomitant tapeworm treatment is indicated.

#### **5. CONTRAINDICATIONS**

Do not use in dogs weighing less than 2.5 kg.  
Do not use in case of hypersensitivity to the active substances or to any of the excipients.  
See also point "Special precautions for use".

#### **6. ADVERSE REACTIONS**

In very rare occasions, 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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

## **7. TARGET SPECIES**

Dogs

## **8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION**

Minimum recommended dose rate: 0.5 mg of milbemycin oxime and 5 mg of praziquantel per kg are given once orally.

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

<b>Weight</b>	<b>Tablets</b>
> 2.5kg – 5 kg	½ tablet
> 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, Milbetab Flavoured Tablets for Dogs 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 Milbetab Flavoured Tablets for Dogs 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, Milbetab Flavoured Tablets for Dogs can replace the monovalent product containing milbemycin oxime alone.

## **9. ADVICE ON CORRECT ADMINISTRATION**

The product should be administered with or after some food.

## **10. WITHDRAWAL PERIOD(S)**

N/A

## **11. SPECIAL STORAGE PRECAUTIONS**

Do not store above 25°C.

Keep blister in the outer carton to protect from light.

## **12. SPECIAL WARNING(S)**

### **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 developing Heartworm in their blood circulation (microfilaremia) can sometimes lead to the appearance of hypersensitivity reactions that are associated with the release of proteins from dead or dying developing Heartworm and are not a direct toxic effect of the product. The use in dogs suffering from microfilaremia is thus not recommended. A veterinary consultation is advised to exclude the presence of any concurrent infestation of Heartworm. In the case of a positive diagnosis, therapy that treats only adult Heartworms is indicated before administering Milbetab Flavoured Tablets for Dogs.

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.

Do not use in animals with a known sensitivity to the active ingredients or to any of the excipients.

Pregnancy and lactation:

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

Interaction with other medicinal products and other forms of interaction:

Although the concurrent use of Milbetab Flavoured Tablets for Dogs with selamectin is well tolerated, in the absence of further studies, caution should be taken in the case of concurrent use of Milbetab Flavoured Tablets for Dogs and other macrocyclic lactones.

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

For animal treatment only.

Wash hands after use.

Keep out of sight and reach of children.

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.

Overdose (symptoms, emergency procedures, antidotes):

No other signs than those observed at the recommended dose have been observed (see section 6).

Incompatibilities:

Not applicable.

**13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Medicines should not be disposed of via wastewater or household waste>.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

**14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

**15. OTHER INFORMATION>**

2, 4 10, 20, 30, 50 or 100 tablets

Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.