1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbetab 12.5 mg/125 mg Tablets for Dogs
Milbetrin 12.5 mg/125 mg Tabletit koirille (FI)
Milbetrin 12.5 mg/125 mg Comprimes pour chiens pesant au moins 5 kg (FR)
Milbetab (EE, DK)
Milipraz (NO)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substances:
Milbemycin oxime 12.5 mg
Praziquantel 125.0 mg

Excipients:

Qualitative composition of excipients and other constituents
Cellulose, microcrystalline
Croscarmellose sodium
Povidone
Lactose monohydrate
Silica, colloidal anhydrous
Magnesium stearate
Talc
Grilled Meat Flavour
Yeast Extract

A white to off white round shaped tablet with a breakline on one side.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (weighing more than 5 kg).

3.2 Indications for use for each target species

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 3.9 'Administration routes and dosage.'
Thelazia callipaeda (see specific treatment schedule under section 3.9 'Administration routes and dosage.'

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

3.3 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 section 3.5 Special precautions for use.

3.4 Special warnings

The use of the veterinary medicinal product should follow the implementation of appropriate diagnostic measures towards mixed infections by nematodes and cestodes with consideration of animal history and characteristics (e.g. age, health status), environment (e.g. kennelled dogs, hunting dogs), feeding (e.g. access to raw meat), geographical location and travel. Judgement of the administration of the veterinary medicinal product in dogs at risk from mixed re-infections or in specific at risk situations (such as zoonotic risks), should be made by the veterinarian responsible.

It is recommended to treat all the animals in the same household concomitantly.
In order to develop an effective worm control programme 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.

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

3.5 Special precautions for use

Special precautions for safe use in the 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 the veterinary medicinal 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 in point 3.10).

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 veterinary medicinal 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 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 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.

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

Wash hands after use.

In case of accidental ingestion, particularly by a child, seek medical advice immediately and show the package leaflet or the label to the physician.
People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment:

See section 5.5.

Other precautions:
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.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Digestive tract disorders (e.g. Diarrhoea, drooling, emesis) Neurological disorders (e.g. Ataxia, muscle tremor) Systemic disorders (e.g. Anorexia, lethargy).

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 respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Can be used during pregnancy and lactation.

Fertility:
Can be used in breeding animals.

3.8 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 veterinary medicinal product 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.

3.9 Administration routes and dosage

For oral use.
Minimum recommended dose rate: 0.5 mg of milbemycin oxime and 5 mg of praziquantel per kg are given once orally.
The veterinary medicinal product should be administered with or after some food.

As per good veterinary practice, animals should be weighed to ensure accurate dosing.
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 veterinary medicinal 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 veterinary medicinal product and continue with the monovalent product containing milbemycin oxime alone, for the remaining three weekly treatments.

In endemic areas administration of the veterinary medicinal 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 veterinary medicinal product can replace the monovalent product containing milbemycin oxime alone.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No other signs than those observed at the recommended dose have been observed (see 3.6).

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QP54A B51

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

After oral administration of praziquantel in the dog, peak serum levels are rapidly attained (T_{max} approximately 2 hours) and decline quickly (t1/2 approximately 2.5 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 occurs at 3.4 hours, and decline with a half-life of the unmetabolised milbemycin oxime of 1.5 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

5.3 Special precautions for storage

Do not store above 25 °C.
Keep blister in the outer carton to protect from light.

5.4 Nature and composition of immediate packaging

Blister packs made up of a cold form laminate of OPA/ALU/PVC and a 20µm hard temper aluminium foil.
Cardboard box with 2 (1 blister strip of 2), 4 (1 blister strip of 4 or 2 blister strips of 2), 8 (1 blister strip of 8, 2 blister strips of 4 or 4 blister strips of 2) 10 (1 blister strip of 10), 20 (10 blister strips of 2

or 2 blister strips of 10), 30 (3 blister strips of 10), 50 (5 blister strips of 10), 100 (10 blister strips of 10), 200 (20 blister strips of 10) or 500 tablets (50 blister strips of 10).
Multipacks of 10 individual packs of 2 tablets, 10 individual packs of 20 tablets and 10 individual packs of 50 tablets.
Not all pack sizes may be marketed.

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

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

The veterinary medicinal product should not enter water courses as milbemycin oxime may be dangerous for fish and other aquatic organisms.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Limited.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: <{DD/MM/YYYY}> <{DD month YYYY}.>

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Veterinary medicinal product not subject to prescription. (NL)
Veterinary medicinal product subject to prescription except for some pack sizes. (FR)

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{Carton}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbetab 12.5 mg/125 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Milbemycin oxime 12.5 mg
Praziquantel 125.0 mg

3. PACKAGE SIZE

2, 4, 8, 10, 20, 30, 50, 100, 200 or 500

4. TARGET SPECIES

Dogs (weighing more than 5 kg)

5. INDICATIONS

For products not subject to veterinary prescription :
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.

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 °C.
Keep blister in the outer carton to protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Limited.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{ BLISTERS }

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbetab

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each tablet contains:
Milbemycin oxime 12.5 mg
Praziquantel 125.0 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Milbetab 12.5 mg/125 mg Tablets for Dogs
Milbetrin 12.5 mg/125 mg Tabletit koirille (FI)
Milbetrin 12.5 mg/125 mg Comprimes pour chiens pesant au moins 5 kg (FR)
Milbetab (EE, DK)
Milipraz (NO)

2. Composition

Each tablet contains:
Active substances:
Milbemycin oxime 12.5 mg
Praziquantel 125.0 mg

A white to off white round shaped tablet with a breakline on one side.

3. Target species

Dogs (weighing more than 5 kg)

4. Indications for use

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 tapeworm treatment is also indicated.

-Tapeworms:
Dipylidium caninum
Taenia spp.
Echinococcus spp.
Mesocestoides spp.

-Roundworms, hookworms and whipworms:
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
Dirofilaria immitis

5. 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".

6. Special warnings

Special warnings:
The use of the veterinary medicinal product should follow the implementation of appropriate diagnostic measures towards mixed infections by nematodes and cestodes with consideration of animal history and characteristics (e.g. age, health status), environment (e.g. kennelled dogs, hunting dogs), feeding (e.g. access to raw meat), geographical location and travel. Judgement of the administration of the veterinary medicinal product in dogs at risk from mixed re-infections or in specific at risk situations (such as zoonotic risks), should be made by the veterinarian responsible.

It is recommended to treat all the animals in the same household concomitantly.
In order to develop an effective worm control programme 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.

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

Special precautions for safe use in the target species:
Studies with one of the active ingredients (milbemycin oxime) in this combination product 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 veterinary medicinal 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 below).

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.

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 veterinary medicinal product, 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 the 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 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
For animal treatment only.
Wash hands after use.

In case of accidental ingestion, particularly by a child, seek medical advice immediately and show the package leaflet or the label to the physician.
People with known hypersensitivity to any of the ingredients should avoid contact with the veterinary medicinal product.

Pregnancy and lactation:
Can be used during pregnancy and lactation.

Fertility:
Can be used in breeding animals.

Interaction with other medicinal products and other forms of interaction:
Although the concurrent use of the veterinary medicinal product with selamectin is well tolerated, in the absence of further studies, caution should be taken in the case of concurrent use of the product and other macrocyclic lactones.

Overdose:
No other signs than those observed at the recommended dose have been observed (see section: Adverse events).

Other Precautions
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.

7. Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Digestive tract disorders (e.g. Diarrhoea, drooling, emesis (Vomiting)) Neurological disorders (e.g. Ataxia (incoordination) and muscle tremors) Systemic disorders (e.g. Anorexia (loss of appetite) and lethargy).

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or its local representative> using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

For oral use.
Minimum recommended dose rate: 0.5 mg of milbemycin oxime and 5 mg of praziquantel per kg are given once orally.
As per good veterinary practice, animals should be weighed to ensure accurate dosing. Depending on the bodyweight of the dog, the recommended dose 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 veterinary medicinal 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 veterinary medicinal product and continue with the monovalent product containing milbemycin oxime alone, for the remaining three weekly treatments.

In endemic areas administration of the veterinary medicinal 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 veterinary medicinal product can replace the monovalent product containing milbemycin oxime alone.

9. Advice on correct administration

The veterinary medicinal product should be administered with or after some food.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Do not store above 25 °C.
Keep blister in the outer carton to protect from light.
Keep out of sight and reach of children.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton/blister after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

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

This veterinary medicinal product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.
Veterinary medicinal product not subject to prescription. (NL)
Veterinary medicinal product subject to prescription except for some pack sizes. (FR)

14. Marketing authorisation numbers and pack sizes

Pack size: 2, 4, 8, 10, 20, 30, 50,100, 200 or 500 tablets.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder <,> <and> <manufacturer responsible for batch release> <and contact details to report suspected adverse events>:
Chanelle Pharmaceuticals Manufacturing Ltd.
Dublin Road
Loughrea
Co. Galway
Ireland
Tel: + 353 91 841788

<Local representatives <and contact details to report suspected adverse events>:>

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

<17. Other information>