ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbepar 4 mg / 10 mg film-coated tablets for small cats and kittens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substances:
Milbemycin oxime 4 mg
Praziquantel 10 mg

Excipients:

Qualitative composition of excipients and other constituents
Core:
Povidone
Croscarmellose sodium
Chicken flavour*
Lactose monohydrate
Cellulose microcrystalline
Silica, colloidal anhydrous
Magnesium stearate
Coat:
Polyvinyl alcohol (E1203)
Titanium dioxide (E171)
Macrogol (E1521)
Talc (E553b)
Iron oxide yellow (E172)

**Artificial origin*

Oblong tablet, beige to yellowish brown, scored on one side. The tablet can be divided into two equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Cats weighing at least 0.5 kg

3.2 Indications for use for each target species

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

- Cestodes:
  Dipylidium caninum
  Taenia spp.

Echinococcus multilocularis

- Nematodes:
Ancylostoma tubaeforme
Toxocara cati

Prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated.

3.3 Contraindications

Do not use in cats of less than 6 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.

3.4 Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infection based on its epidemiological features, for each individual animal.
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.
Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class.
It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method. Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.
The use of this product should take into account local information about susceptibility of the target parasites, where available.
In the absence of risk of co-infection with nematodes or cestodes, a narrow spectrum product should be used.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Ensure cats and kittens weighing between 0.5 kg and ≤2 kg receive the appropriate tablet strength (4 mg milbemycin oxime / 10 mg praziquantel) and the appropriate dose (1/2 or 1 tablet) for the corresponding weight band (1/2 tablet for cats weighing 0.5 to 1 kg ; 1 tablet for cats weighing >1 to 2 kg).

No studies have been performed with severely debilitated cats 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.
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may be harmful when ingested, particularly for children. To avoid accidental ingestion, the product should be stored out of sight and reach of children. Any unused tablet parts should be returned in the opened blister, inserted back into the outer packaging and used at the next administration or securely discarded (see section 5.5).

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.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

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 (e.g., experts or institutes of parasitology).

3.6 Adverse events

Cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction[1] Systemic disorders[1] (e.g. Lethargy) Neurological signs[1] (e.g. Ataxia, Muscle tremor) Digestive tract disorders[1] (e.g. Emesis, Diarrhoea)

[1]: especially in young cats

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

Fertility
Can be used in breeding cats.

3.8 Interaction with other medicinal products and other forms of interaction

The concurrent use of a tablet containing milbemycin oxime and praziquantel with selamectin is well tolerated. No interactions were observed when the recommended dose of the macrocyclic lactone selamectin was administered during treatment with a tablet containing milbemycin oxime and praziquantel at the recommended dose.
Although not recommended, the concomitant use of a tablet containing milbemycin oxime and praziquantel with a spot-on containing moxidectin and imidacloprid at recommended dose rates following a single application was well tolerated in one laboratory study in 10 kittens.
The safety and efficacy of the concurrent use have not been investigated in field studies. In the absence of further studies, caution should be taken in the case of concurrent use of a tablet containing

milbemycin oxime and praziquantel with any other macrocyclic lactone. Also, no such studies have been performed with reproducing animals.

3.9 Administration routes and dosage

Oral use.
Minimum recommended dose rate: 2 mg of milbemycin oxime and 5 mg of praziquantel per kg are given orally as a single dose.
Animals should be weighed to ensure accurate dosing. Depending on the bodyweight of the cat, the practical dosing is as follows:

Body weight (kg)	4 mg /10 mg film-coated tablets
0.5-1	1/2 tablet
>1-2	1 tablet

The veterinary medicinal product should be administered with or after some food. Doing so ensures optimal protection against heartworm disease.
The product can be inserted into a program for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. The product has a duration of heartworm prevention of one month. For regular prevention of heartworm disease, the use of a monosubstance is preferred.
Underdosing could result in ineffective use and may favour resistance development.
The need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

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

In case of overdose, in addition to signs observed at the recommended dose (see section 3.6 Adverse events), drooling was observed. This sign will usually disappear spontaneously within a day.

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 :

QP54AB51

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 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 . 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 depolarization andalmost 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

In the cat, plasma concentrations of praziquantel reach a peak of 1225 µg/L within 2 hours after oral administration. The half-life of elimination is around 4 hours. After oral administration in the cat, plasma concentrations of milbemycin oxime reach a peak of 1696 µg/L within 3 hours. The half-life of elimination is around 78 hours. 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: 3 years
Shelf life for halved tablet after first opening the blister: 6 months

5.3 Special precautions for storage

Any unused tablet parts should be returned to the opened blister, inserted back into the outer packaging and used at the next administration or securely discarded (see section 5.5)
Protect from light.

5.4 Nature and composition of immediate packaging

Polyamide-Aluminium-Polyvinyl chloride / aluminium heat sealed blisters.
Cardboard box with 1 blister of 2 tablets (2 tablets).
Cardboard box with 2 blisters of 2 tablets (4 tablets).
Cardboard box with 5 blisters of 2 tablets (10 tablets).
Cardboard box with 12 blisters of 2 tablets (24 tablets).
Cardboard box with 24 blisters of 2 tablets (48 tablets).
Cardboard box with 50 blisters of 2 tablets (100 tablets).

Not all pack sizes may be marketed.

5.5 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 or household waste.
The 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 national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

IE: Veterinary medicinal product subject to prescription.
FR: Veterinary medicinal product subject to prescription except for some pack sizes.

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

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbepar 4 mg / 10 mg film-coated tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Milbemycin oxime 4 mg/tablet
Praziquantel 10 mg/tablet

3. PACKAGE SIZE

2 tablets
4 tablets
10 tablets
24 tablets
48 tablets
100 tablets

4. TARGET SPECIES

Cats weighing at least 0.5 kg

5. INDICATIONS

For pack sizes not subject to veterinary prescription:
For the treatment of mixed infections by adult cestodes and nematodes and the prevention of heartworm disease in cats if concomitant treatment against cestodes is indicated.
Recommended for small cats between 0.5 and 2 kg body weight according to the dosing table below:

Body weight (kg)	4 mg/10 mg tablets
0.5-1	1/2 tablet
>1-2	1 tablet

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life for halved tablet after first opening the blister: 6 months.

9. SPECIAL STORAGE PRECAUTIONS

Any unused tablet parts should be returned to the opened blister, inserted back into the outer packaging and used at the next administration or securely discarded.
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

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbepar

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

4 mg milbemycin oxime and 10 mg praziquantel per tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Milbepar 4 mg / 10 mg film-coated tablets for small cats and kittens

2. Composition

Each tablet contains:
Active substances:
Milbemycin oxime 4 mg
Praziquantel 10 mg

Oblong tablet, beige to yellowish brown, scored on one side. The tablet can be divided into two equal parts.

3. Target species

Cats weighing at least 0.5 kg

4. Indications for use

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

- Cestodes:
  Dipylidium caninum
  Taenia spp.
  Echinococcus multilocularis

- Nematodes:
  Ancylostoma tubaeforme
  Toxocara cati

Prevention of heartworm disease (*Dirofilaria immitis*) if concomitant treatment against cestodes is indicated.

5. Contraindications

Do not use in cats of less than 6 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.

6. Special warnings

Special warnings:
Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infection based on its epidemiological features, for each individual animal.
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.
Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class.
It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method. Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.
The use of this product should take into account local information about susceptibility of the target parasites, where available.
In the absence of risk of co-infection with nematodes or cestodes, a narrow spectrum product should be used.

Special precautions for safe use in the target species:
Ensure cats and kittens weighing between 0.5 kg and ≤2 kg receive the appropriate tablet strength (4 mg milbemycin oxime / 10 mg praziquantel) and the appropriate dose (1/2 or 1 tablet) for the corresponding weight band (1/2 tablet for cats weighing 0.5 to 1 kg; 1 tablet for cats weighing >1 to 2 kg).

No studies have been performed with severely debilitated cats 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.
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may be harmful when ingested, particularly for children. To avoid accidental ingestion, the product should be stored out of sight and reach of children. Any unused tablet parts should be returned in the opened blister, inserted back into the outer packaging and be used at the next administration or securely discarded (see section "Special precautions for disposal").
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.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

Pregnancy and lactation:
The safety of the veterinary medicinal product has been established during pregnancy and lactation.
Can be used during pregnancy and lactation.

Fertility
Can be used in breeding cats.

Interaction with other medicinal products and other forms of interaction:
The concurrent use of a tablet containing milbemycin oxime and praziquantel with selamectin is well tolerated. No interactions were observed when the recommended dose of the macrocyclic lactone selamectin was administered during treatment with a tablet containing milbemycin oxime and praziquantel at the recommended dose.
Although not recommended, the concomitant use of a tablet containing milbemycin oxime and praziquantel with a spot on containing moxidectin and imidacloprid at recommended dose rates following a single application was well tolerated in one laboratory study in 10 kittens.
The safety and efficacy of the concurrent use have not been investigated in field studies. In the absence of further studies, caution should be taken in the case of concurrent use of a tablet containing milbemycin oxime and praziquantel with any other macrocyclic lactone. Also, no such studies have been performed with reproducing animals.

Overdose:
In case of overdose, in addition to signs observed at the recommended dose (see section "Adverse events"), drooling was observed. This sign will usually disappear spontaneously within a day.

Special restrictions for use and special conditions for use:
Not applicable.

Major incompatibilities:
Not applicable.

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 (e.g., experts or institutes of parasitology).

7. Adverse events

Cats:

Very rare (< 1 animal / 10,000 animals treated, including isolated reports):
Hypersensitivity reaction[1], Systemic disorders[1] (e.g. Lethargy), Neurological signs[1] (e.g. Ataxia, Muscle tremor), Digestive tract disorders[1] (e.g. Vomiting, Diarrhoea)

[1]: especially in young cats

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal 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 using the contact details at the end of this leaflet, or via your national reporting system.

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

Oral use.
Animals should be weighed to ensure accurate dosing. Minimum recommended dose rate: 2 mg of milbemycin oxime and 5 mg of praziquantel per kg are given orally as a single dose.
Depending on the bodyweight of the cat, the practical dosing is as follows:

Body weight (kg)	4mg/10 mg film-coated tablets
0.5-1	1/2 tablet
>1-2	1 tablet

The veterinary medicinal product can be inserted into a program for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. The product has a duration of heartworm prevention of one month. For regular prevention of heartworm disease, the use of a monosubstance is preferred.
Underdosing could result in ineffective use and may favour resistance development.
The need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

9. Advice on correct administration

The veterinary medicinal product should be administered with or after some food. Doing so ensures optimal protection against heartworm disease.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Any unused tablet parts should be returned to the opened blister, inserted back into the outer packaging and used at the next administration or securely discarded (see section "Special precautions for disposal").

Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and on the blister. The expiry date refers to the last day of that month.

Shelf life for halved tablet after first opening the blister: 6 months.

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

IE: Veterinary medicinal product subject to prescription.
FR: Veterinary medicinal product subject to prescription except for some pack sizes.

14. Marketing authorisation numbers and pack sizes

Cardboard box with 1 blister of 2 tablets (2 tablets).
Cardboard box with 2 blisters of 2 tablets (4 tablets).
Cardboard box with 5 blisters of 2 tablets (10 tablets).
Cardboard box with 12 blisters of 2 tablets (24 tablets).
Cardboard box with 24 blisters of 2 tablets (48 tablets).
Cardboard box with 50 blisters of 2 tablets (100 tablets).
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{dd/mm/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 contact details to report suspected adverse reactions:
Tel: +800 35 22 11 51
Email: pharmacovigilance@ceva.com

Manufacturer responsible for batch release:
Ceva Santé Animale, Boulevard de la Communication, Zone Autoroutière, 53950 Louverné, France

17. Other information