ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Milbemax 16 mg/40 mg film-coated tablets for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:
Milbemycin oxime 16 mg
Praziquantel 40 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Core:	
Cellulose, microcristalline	
Magnesium stearate	
Croscarmellose sodium	
Povidone	
Lactose monohydrate	
Silica, colloidal anhydrous	
Coat:	
Hypromellose	
Macrogol 8000	
Talc	
Iron oxide red (E172)	0.213 mg
Artificial beef flavour	

Oblong shaped, reddish to reddish brown, artificial beef flavoured film-coated tablet with a score on both sides. One side bears the imprint “KK”, the other side “NA”.

3. CLINICAL INFORMATION

3.1 Target species

Cats (≥ 2 kg).

3.2 Indications for use for each target species

For cats with, or at risk from mixed infections of cestodes, gastrointestinal nematodes, and/or heartworm. This veterinary medicinal product is only indicated when use against cestodes and nematodes or prevention of heartworm disease is indicated at the same time.

Cestodes
Treatment of tapeworms:

Dipylidium caninum,
Taenia spp.*,*
Echinococcus multilocularis.

Gastrointestinal nematodes
Treatment of:
Hookworm: *Ancylostoma tubaeforme,*
Roundworm: *Toxocara cati.*

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

3.3 Contraindications

Do not use in cats weighing less than 2 kg.
Do not use in cases of hypersensitivity to the active substances or to any of excipients.

3.4 Special warnings

The possibility that other animals in the same household can be a source of re-infection should be considered, and these should be treated as necessary with an appropriate veterinary medicinal product. 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.
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 veterinary medicinal 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.

In the absence of risk of co-infection with nematodes or cestodes, a narrow spectrum veterinary medicinal product should be used when available.

The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available.

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 MBO/10 mg praziquantel) and the appropriate dose. See also section 3.9.

No studies have been performed with severely debilitated cats 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use.
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 physician.

Special precautions for the protection of the environment:
See section 5.5.

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):	Digestive tract disorders (such as Diarrhoea, Emesis) Hypersensitivity reaction Neurological disorders (such as Ataxia and Muscle tremor) Systemic disorders (such as 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

The concurrent use of the veterinary medicinal product with selamectin is well tolerated. 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. Although not recommended, the concomitant use of the veterinary medicinal product 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 with any other macrocyclic lactone. Also, no such studies have been performed with breeding animals.

3.9 Administration routes and dosage

Oral use.
Underdosing could result in ineffective use and may favour resistance development.
To ensure a correct dosage, body weight should be determined as accurately as possible.
Minimum recommended dose rate: 2 mg of milbemycin oxime and 5 mg of praziquantel per kg are given as a single dose. The veterinary medicinal product should be administered with or after some food. Doing so ensures optimum protection against heartworm disease.

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

Weight	Tablets
2 - 4 kg	½ tablet
> 4 - 8 kg	1 tablet
> 8 - 12 kg	1½ tablets

The veterinary medicinal product can be inserted into a programme for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. The duration of heartworm prevention is one month. For regular prevention of heartworm disease the use of a monosubstance is preferred.

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 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.

4.3 Pharmacokinetics

In the cat, praziquantel reaches peak plasma concentrations within an hour after oral administration. The half-life of elimination is around 3 hours.
In the dog, there is rapid hepatic biotransformation, principally to monohydroxylated derivatives. The principal route of elimination in the dog is renal.

After oral administration in the cat, milbemycin oxime reaches peak plasma concentrations within 2 hours. The half-life of elimination is around 13 hours (± 9 hours).
In the rat, metabolism appears to be complete although slow, since unchanged milbemycin oxime has not been found in urine or feces. 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: 3 years.
Shelf-life after first opening of the immediate packaging: 6 months (half tablet).

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

PVC/PE/PVdC/aluminium blisters in an outer cardboard box.

Cardboard box with 1 blister of 2 or 4 film-coated tablets.
Cardboard box with 1, 2, 5 or 10 blisters of 10 film-coated 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 it 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

Elanco

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: DD/MM/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. [AT, CY, CZ, DE, DK, EL, ES, FI, HU, IE, IT, NI, NO, PL, PT, SI, SK]
Veterinary medicinal product not subject to prescription. [BE, LU, NL]
Veterinary medicinal product subject to prescription except for some pack sizes. [FR, SE]

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

Milbemax 16 mg/40 mg film-coated tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Milbemycin oxime	16 mg/film-coated tablet
Praziquantel	40 mg/film-coated tablet

3. PACKAGE SIZE

2 tablets
4 tablets
10 tablets
20 tablets
50 tablets
100 tablets

4. TARGET SPECIES

Cats (≥ 2 kg).

5. INDICATIONS

For products not subject to veterinary prescription
Treatment of mixed infections by tapeworms, hookworm and roundworm.
Prevention of heartworm infection if concomitant treatment against cestodes is indicated.

Weight	Dosage
2 – 4 kg	½ tablet
> 4 – 8 kg	1 tablet
> 8 – 12 kg	1 ½ tablets

Single oral administration with or after some food.

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 6 months (half tablet).

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.
Keep the blister in the outer carton in order 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

Elanco logo

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

Milbemax (≥ 2 kg)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

16 mg/40 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Milbemax 16 mg/40 mg film-coated tablets for cats
Milbemax 4 mg/10 mg film-coated tablets for small cats and kittens

2. Composition

This veterinary medicinal product is available in 2 different sizes:

Name of Tablet (Type of Tablet)	Milbemycin oxime per tablet	Praziquantel per tablet	Excipient (Iron oxide red (E172))	Imprint
Milbemax 4 mg/10 mg film-coated tablets for small cats and kittens (beige to brown, artificial beef flavoured, oblong, divisible)	4 mg	10 mg	n/a	One side "BC", the other side "NA".
Milbemax 16 mg/40 mg film-coated tablets for cats (reddish to reddish brown, artificial beef flavoured, oblong, divisible)	16 mg	40 mg	0.213 mg	One side "KK", the other side "NA".

3. Target species

Cats.

4. Indications for use

For cats with, or at risk from mixed infections of cestodes, gastrointestinal nematodes, and/or heartworm. This veterinary medicinal product is only indicated when use against cestodes and nematodes or prevention of heartworm disease is indicated at the same time.

Cestodes
Treatment of tapeworms:
Dipylidium caninum,
Taenia spp.*,*
Echinococcus multilocularis.

Gastrointestinal nematodes
Treatment of:
Hookworm: *Ancylostoma tubaeforme,*
Roundworm: *Toxocara cati.*

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

5. Contraindications

Do not use the '**tablets for small cats and kittens'** in cats of less than 6 weeks of age and/or weighing less than 0.5 kg.
Do not use the '**tablets for cats'** in cats weighing less than 2 kg.
Do not use in cases of hypersensitivity to the active substances or to any of excipients.

6. Special warnings

Special warnings:
The possibility that other animals in the same household can be a source of re-infection should be considered, and these should be treated as necessary with an appropriate veterinary medicinal product. 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.
Unnecessary use of antiparasitics or use deviating from the instructions given in the package leaflet may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the veterinary medicinal 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.
In the absence of risk of co-infection with nematodes or cestodes, a narrow spectrum veterinary medicinal product should be used when available.
The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available.

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 MBO/10 mg praziquantel) and the appropriate dose. See also section "Dosage for each species, routes and method of administration".
No studies have been performed with severely debilitated cats 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use.
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 physician.

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:
The concurrent use of the veterinary medicinal product with selamectin is well tolerated. 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.
Although not recommended, the concomitant use of the veterinary medicinal product 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 with any other macrocyclic lactone. Also, no such studies have been performed with breeding 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 precautions for the protection of the environment:
See Special precautions for disposal.

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):	Digestive tract disorders (such as Diarrhoea, Emesis (Vomiting)) Hypersensitivity reaction Neurological disorders (such as Ataxia (Incoordination) and Muscle tremor) Systemic disorders (such as Lethargy)

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 or the local representative of 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.
Underdosing could result in ineffective use and may favour resistance development.
To ensure a correct dosage, body weight should be determined as accurately as possible.
The veterinary medicinal product is administered at a minimum recommended dose rate of 2 mg milbemycin oxime and 5 mg praziquantel per kg body weight as a single dose.

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

Weight	**Milbemax 4 mg/10 mg film-coated tablets for small cats and kittens**	**Milbemax 16 mg/40 mg film-coated tablets for cats**
0.5 – 1 kg	½ tablet	
> 1 – 2 kg	1 tablet	
≥ 2 – 4 kg		½ tablet
> 4 – 8 kg		1 tablet
> 8 – 12 kg		1 ½ tablets

The veterinary medicinal product can be inserted into a programme for prevention of heartworm disease if at the same time treatment against tapeworms is indicated. The duration of heartworm prevention is one month. For regular prevention of heartworm disease the use of a monosubstance is preferred.

9. Advice on correct administration

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

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25°C.
Keep the blister in the outer carton in order to protect from light.
Do not use after the expiry date stated on the blister and carton after Exp. The expiry date refers to the last day of that month.
Shelf-life after first opening of the immediate packaging: 6 months (half tablet).

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 it 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. [AT, CY, CZ, DE, DK, EL, ES, FI, HU, IE, IT, NI, NO, PL, PT, SI, SK]
Veterinary medicinal product not subject to prescription. [BE, LU, NL]
Veterinary medicinal product subject to prescription except for some pack sizes. [FR, SE]

14. Marketing authorisation numbers and pack sizes

PVC/PE/PVdC/aluminium blisters in an outer cardboard box.

Cardboard box with 1 blister of 2 or 4 film-coated tablets.
Cardboard box with 1, 2, 5 or 10 blisters of 10 film-coated tablets.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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:

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 rue de la Chapelle, F-68330 Huningue, France

Local representatives and contact details to report suspected adverse reactions: