

## **ANNEX I**

### **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alpramil 12 mg/30 mg film-coated tablets for cats weighing at least 3 kg (AT, BE, BG, CY, CZ, DE, EE, EL, ES, FR, HU, HR, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI))

Alpramil Vet 12 mg/30 mg film-coated tablets for cats weighing at least 3 kg (DK, FI, IS, NO, SE)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

### Active substances:

Milbemycin oxime 12.0 mg

Praziquantel 30.0 mg

### Excipients:

| Qualitative composition of excipients and other constituents | Quantitative composition if that information is essential for proper administration of the veterinary medicinal product |
|--|---|
| <i>Core:</i>   |   |
| Povidone   |   |
| Cellulose, microcrystalline                                  |   |
| Croscarmellose sodium  |   |
| Lactose monohydrate  |   |
| Silica, colloidal hydrated                                   |   |
| Magnesium stearate   |   |
| <i>Coat:</i>   |   |
| Hypromellose   |   |
| Lactose monohydrate  |   |
| Titanium dioxide (E171)                                      | 0.456 mg  |
| Macrogol   |   |
| Vanillin   |   |
| Iron oxide yellow (E172)                                     | 0.157 mg  |
| Iron oxide red (E172)  | 0.024 mg  |

Oblong and convex orange film-coated tablet.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cats weighing at least 3 kg.

### 3.2 Indications for use for each target species

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 weighing less than 3 kg.  
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

### 3.4 Special warnings

In order to develop an effective worm control programme local epidemiological information and the risk of exposure of the cat should be taken into account.

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. Unnecessary use of antiparasitics or use deviating from the instructions may increase the resistance selection pressure and lead to reduced efficacy.

### 3.5 Special precautions for use

#### Special precautions for safe use in the target species:

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:

This veterinary medicinal product may be harmful when ingested, particularly for children.

Avoid accidental ingestion.

The veterinary medicinal product should be stored in a safe place.

In case of accidental ingestion, 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.

### 3.6 Adverse events

Cats:

|   |  |
|---|--|
| Very rare<br>(<1 animal / 10,000 animals treated,<br>including isolated reports): | Hypersensitivity reaction <sup>1</sup> ;<br>Systemic disorders (e.g. lethargy) <sup>1</sup> ;<br>Neurological disorders (e.g. muscle tremor and ataxia) <sup>1</sup> ;<br>Digestive tract disorders (e.g. emesis and diarrhoea) <sup>1</sup> . |
|---|--|

<sup>1</sup> 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 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 of the veterinary medicinal product with any other macrocyclic lactone. Also, no such studies have been performed with reproducing animals.

### 3.9 Administration routes and dosage



Oral use.

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 orally 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 and the availability of tablet strengths, practical dosing examples are as follows:

| Weight (kg) | 12 mg/30 mg tablet  |           |
|-------------|---|-----------|
| > 3 – 6     |  | 1 tablet  |
| > 6 – 12    |  | 2 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 veterinary medicinal product has a duration of heartworm prevention of 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), 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<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.

### **4.3 Pharmacokinetics**

After oral administration, praziquantel reaches peak plasma concentrations (C<sub>max</sub> 1.08 µg/ml) within 2 hours after oral administration. The half-life of elimination is around 2 hours.

After oral administration, milbemycin oxime reaches peak plasma concentrations (C<sub>max</sub> 1.48 µg/ml) within 3 hours. The half-life of elimination is around 22 hours (± 10 hours).

## **5. PHARMACEUTICAL PARTICULARS**

### **5.1 Major incompatibilities**

Not applicable.

### **5.2 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

### **5.3 Special precautions for storage**

This veterinary medicinal product does not require any special storage conditions.

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

PVC / PE / PVDC - Aluminium blisters containing 1, 2 or 4 tablets.

Box with 1 blister containing 1 tablet.

Box with 1 blister containing 2 tablets.

Box with 1 blister containing 4 tablets.

Box with 10 blisters each containing 1 tablet.

Box with 10 blisters each containing 2 tablets.

Box with 10 blisters each containing 4 tablets.

Box with 25 blisters each containing 1 tablet.

Box with 25 blisters each containing 2 tablets.

Box with 25 blisters each containing 4 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**

Alfasan Nederland B.V.

### **7. MARKETING AUTHORISATION NUMBER(S)**

### **8. 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 (DE, DK, EE, EL, FI, HR, IE, NO, PL, SI, UK(NI)).

Veterinary medicinal product not subject to prescription (AT, BE, BG, CY, CZ, ES, FR, HU, IS, IT, LT, LU, LV, NL, PT, RO, SE, SK).

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

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**



**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARTON BOX**

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

Alpramil 12 mg/30 mg film-coated tablets

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each tablet contains: milbemycin oxime 12.0 mg and praziquantel 30.0 mg.

**3. PACKAGE SIZE**

1 tablet  
2 tablets  
4 tablets  
10 tablets  
20 tablets  
25 tablets  
40 tablets  
50 tablets  
100 tablets

**4. TARGET SPECIES**

Cats weighing at least 3 kg.



**5. INDICATIONS**

*For products not subject to veterinary prescription: To be completed nationally.*

**6. ROUTES OF ADMINISTRATION**

Oral use.

**7. WITHDRAWAL PERIODS**

**8. EXPIRY DATE**

Exp. {mm/yyyy}

**9. SPECIAL STORAGE PRECAUTIONS**

**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**

Alfasan Nederland B.V.

**14. MARKETING AUTHORISATION NUMBERS**

**15. BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS****PVC / PE / PVDC / Aluminium blisters****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Alpramil

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

12 mg milbemycin oxime /30 mg praziquantel/tablet

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Alpramil 4 mg/10 mg film-coated tablets for cats weighing at least 0.5 kg

Alpramil 12 mg/30 mg film-coated tablets for cats weighing at least 3 kg

Alpramil 16 mg/40 mg film-coated tablets for cats weighing at least 4 kg

### 2. Composition

Each 4 mg/10 mg tablet contains:

#### Active substances:

|                  |         |
|------------------|---------|
| Milbemycin oxime | 4.0 mg  |
| Praziquantel     | 10.0 mg |

#### Excipients:

|                          |          |
|--------------------------|----------|
| Titanium dioxide (E171)  | 0.186 mg |
| Quinoline Yellow (E104)  | 0.023 mg |
| Sunset Yellow FCF (E110) | 0.004 mg |

Round and convex yellow film-coated tablet with a break line on one side.

Tablets can be divided into halves.

Each 12 mg/30 mg tablet contains:

#### Active substances:

|                  |         |
|------------------|---------|
| Milbemycin oxime | 12.0 mg |
| Praziquantel     | 30.0 mg |

#### Excipients:

|                          |          |
|--------------------------|----------|
| Titanium dioxide (E171)  | 0.456 mg |
| Iron oxide yellow (E172) | 0.157 mg |
| Iron oxide red (E172)    | 0.024 mg |

Oblong and convex orange film-coated tablet.

Each 16 mg/40 mg tablet contains:

#### Active substances:

|                  |         |
|------------------|---------|
| Milbemycin oxime | 16.0 mg |
| Praziquantel     | 40.0 mg |

#### Excipients:

|                         |          |
|-------------------------|----------|
| Titanium dioxide (E171) | 0.711 mg |
| Iron oxide red (E172)   | 0.069 mg |
| Iron oxide black (E172) | 0.069 mg |

Oblong and convex purple-brown film-coated tablet.

### 3. Target species

4 mg/10 mg tablet: Cats weighing at least 0.5 kg.  
12 mg/30 mg tablet: Cats weighing at least 3 kg.  
16 mg/40 mg tablet: Cats weighing at least 4 kg.



#### **4. Indications for use**

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**

4 mg/10 mg tablet: Do not use in cats of less than 6 weeks of age and/or weighing less than 0.5 kg.

12 mg/30 mg tablet: Do not use in cats weighing less than 3 kg.

16 mg/40 mg tablet: Do not use in cats weighing less than 4 kg.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

#### **6. Special warnings**

##### Special warnings:

In order to develop an effective worm control programme local epidemiological information and the risk of exposure of the cat should be taken into account, and it is recommended to seek professional advice.

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. Unnecessary use of antiparasitics or use deviating from the instructions may increase the resistance selection pressure and lead to reduced efficacy.

##### Special precautions for safe use in the target species:

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:

This veterinary medicinal product may be harmful when ingested, particularly for children.

Avoid accidental ingestion.

Any unused tablet parts of 4 mg/10 mg tablets should be discarded or returned to the open blister, inserted back into the outer packaging and used at the next administration. The veterinary medicinal product should be stored in a safe place.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.  
Wash hands after use.

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.

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 of the veterinary medicinal product 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 Adverse events), drooling was observed. This sign will usually disappear spontaneously within a day.

## **7. Adverse events**

Cats:

|   |  |
|---|--|
| Very rare<br>(<1 animal / 10,000 animals treated,<br>including isolated reports): | Hypersensitivity reaction <sup>1</sup> ;<br>Systemic disorders (e.g. lethargy) <sup>1</sup> ;<br>Neurological disorders (e.g. muscle tremor and ataxia<br>(incoordination)) <sup>1</sup> ;<br>Digestive tract disorders (e.g. emesis (vomiting) and<br>diarrhoea) <sup>1</sup> . |
|---|--|

<sup>1</sup> 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 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: {national system details}.

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





Oral use.

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 orally as a single dose.

Depending on the bodyweight of the cat and the availability of tablet sizes, practical dosing examples are as follows:



4 mg/10 mg tablet:

| Weight (kg) | 4 mg/10 mg tablet   |            |
|-------------|---|------------|
| 0.5 – 1     |  | ½ tablet   |
| > 1 – 2     |  | 1 tablet   |
| > 2 – 3     |  | 1½ tablets |
| > 3 – 4     |  | 2 tablets  |

12 mg/30 mg tablet:

| Weight (kg) | 12 mg/30 mg tablet  |           |
|-------------|---|-----------|
| > 3 – 6     |  | 1 tablet  |
| > 6 – 12    |  | 2 tablets |

16 mg/40 mg tablet:

| Weight (kg) | 16 mg/40 mg tablet  |           |
|-------------|---|-----------|
| > 4 – 8     |  | 1 tablet  |
| > 8 – 16    |  | 2 tablets |

## 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.

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 veterinary medicinal product has a duration of heartworm prevention of one month. For regular prevention of heartworm disease, the use of a monosubstance is preferred.

## 10. Withdrawal periods

Not applicable.

## 11. Special storage precautions

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

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

4 mg/10 mg tablet: Shelf life of divided tablets after first opening the immediate packaging: 7 days.



## **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 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 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 (DE, DK, EE, EL, FI, HR, IE, NO, PL, SI, UK(NI)).

Veterinary medicinal product not subject to prescription (AT, BE, BG, CY, CZ, ES, FR, HU, IS, IT, LT, LU, LV, NL, PT, RO, SE, SK).

## **14. Marketing authorisation numbers and pack sizes**

PVC/PE/PVDC - Aluminium blisters containing 1, 2 or 4 tablets.

Box with 1 blister containing 1 tablet.

Box with 1 blister containing 2 tablets.

Box with 1 blister containing 4 tablets.

Box with 10 blisters each containing 1 tablet.

Box with 10 blisters each containing 2 tablets.

Box with 10 blisters each containing 4 tablets.

Box with 25 blisters each containing 1 tablet.

Box with 25 blisters each containing 2 tablets.

Box with 25 blisters each containing 4 tablets.

Not all pack sizes may be marketed.

## **15. Date on which the package leaflet was last revised**

{DD/MM/YYYY}.

## **16. Contact details**

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:

Alfasan Nederland B.V.

Kuipersweg 9

3449 JA Woerden

The Netherlands

Tel: +31(0)348 416945

Manufacturer responsible for batch release:

LelyPharma B.V.

Zuiveringsweg 42

8243 PZ Lelystad

The Netherlands

Local representatives and contact details to report suspected adverse reactions:

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

**17. Other information**