SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
Round and convex yellow coated tablet with a break line on one side.
Tablets can be divided into halves.

4. CLINICAL PARTICULARS

4.1 Target species

Cats weighing at least 0.5 kg

4.2 Indications for use, specifying the 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.

4.3 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 known cases of hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings for each target species

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.

4.5 Special precautions for use

Special precautions for use in animals
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.

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 should be discarded or returned to the open blister, inserted back into the outer packaging and used at the next administration. The 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 (OIE), specific guidelines on the treatment and follow-up and on the safeguard of persons need to be obtained from the relevant competent authority.

4.6 Adverse reactions (frequency and seriousness)

On very rare occasions, especially in young cats, hypersensitivity reactions, systemic signs (such as lethargy), neurological signs (such as ataxia and muscle tremors) and/or gastrointestinal signs (such as emesis and diarrhoea) have been observed after administration of the veterinary medicinal product.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The product can be used in breeding cats including pregnant and lactating queens.

4.8 Interaction with other medicinal products and other forms of interaction

The concurrent use of the 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 product at the recommended dose.
Although not recommended, the concomitant use of the 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 product with any other macrocyclic lactone. Also, no such studies have been performed with reproducing animals.

4.9 Amounts to be administered and administration route

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

Animals should be weighed to ensure accurate dosing. Depending on the bodyweight of the cat and the availability of tablet strengths, practical dosing examples are as follows:

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

The product can be inserted into a programme 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.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In case of overdose, in addition to signs observed at the recommended dose (see section 4.6), drooling was observed. This sign will usually disappear spontaneously within a day.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Endectocides, macrocyclic lactones (milbemycin oxime, combinations)
ATC vet code: QP54AB51

5.1 Pharmacodynamic properties

Milbemycin oxime belongs to the group of macrocyclic lactones, isolated from the fermentation of *Streptomyces hygroscopicus* var. *aureolacrimosus*. It is active against mites, against larval and adult stages of nematodes as well as against larvae of *Dirofilaria immitis*.
The activity of milbemycin is related to its action on invertebrate neurotransmission: Milbemycin oxime, like avermectins and other milbemycins, increases nematode and insect membrane permeability to chloride ions via glutamate-gated chloride ion channels (related to vertebrate $GABA_A$ 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.

5.2 Pharmacokinetic particulars

After oral administration, praziquantel reaches peak plasma concentrations (C_{max} 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_{max} 1.48 µg/ml) within 3 hours. The half-life of elimination is around 22 hours (± 10 hours).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Povidone
Cellulose, microcrystalline
Croscarmellose sodium
Lactose monohydrate
Silica, colloidal hydrated
Magnesium stearate

Coat:
Hypromellose
Lactose monohydrate
Titanium dioxide (E171)
Macrogol
Vanillin
Quinoline Yellow (E104)
Sunset Yellow FCF (E110)

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months
Shelf life of divided tablets after first opening the immediate packaging: 7 days

6.4 Special precautions for storage

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

6.5 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.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.
The product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

8. MARKETING AUTHORISATION NUMBER

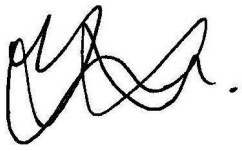
Vm 36408/5001

9. DATE OF FIRST AUTHORISATION

06 May 2022

10. DATE OF REVISION OF THE TEXT

May 2022



Approved: 06 May 2022