SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PROGRAM Plus film-coated tablets 11.5mg/230 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances

Milbemycin oxime	11.5 mg
Lufenuron	230.0 mg

Excipient:

Titanium dioxide (E171)	3.7 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets
White, pentagonal, biconvex, bevel-edged, coated tablets with “GLG” on one side and “CGV” on the reverse.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

PROGRAM Plus is used for the prevention of fleas (*Ct. felis, Ct. canis*, preadult stages), and for the concurrent prevention of heartworm (elimination of L3/L4 larval stages of *Dirofilaria immitis)* and/or treatment of adult stages of gastrointestinal nematodes such as hookworms (*Ancylostoma caninum)*, roundworms (*Toxocara canis)* and whipworms (*Trichuris vulpis*).

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance, to the adjuvants or to any of the excipients.

4.4 Special warnings

Ideally, tablets are administered on the same day each month. If an interval is greater than 6 weeks, treatment should be resumed immediately and be continued at monthly intervals and, in case of heartworm prevention, a veterinarian should be consulted.

4.5 Special precautions for use

i. Special precautions for use in animals

In heartworm risk regions*,* or in case it is known that a dog has been travelling to and from heartworm risk regions, before commencing PROGRAM Plus treatment as with any other heartworm preventive, 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 PROGRAM Plus.

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

None.
In the case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Pale mucous membranes, increased intestinal peristalsis, lethargy, diarrhea have been observed very rarely after treatment. The treatment of dogs with a high number of circulating microfilariae can sometimes lead to the appearance of moderate and transitory hypersensitivity reactions, such as pale mucous membranes, vomiting, 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.

4.7 Use during pregnancy, lactation or lay

Pregnancy:
Can be used during pregnancy.

Lactation:
Can be used during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

During treatment with PROGRAM Plus, no other antiparasitic macrocyclic lactones should be administered.

4.9 Amounts to be administered and administration route

PROGRAM Plus tablets, available in four sizes, are given according to the weight of the dog, consistent with the administration of a minimum dose of 0.5 mg milbemycin oxime and 10 mg lufenuron per kg body weight.

Colour of container	Body weight (kg)	Posology	mg of milbemycin per tablet	mg of lufenuron per tablet
yellow	from 12 to 22 kg	1 tablet/month	11.5	230

PROGRAM Plus should be administered in the following situations:

Puppies:
To prevent flea infestations with concurrent heartworm prevention and/or gastrointestinal nematode infection treatment should start from 2 weeks of age, or from a minimum weight of 1 kg.

Dogs in a non-heartworm region:
Program Plus can be used as part of the seasonal prevention of fleas replacing lufenuron mono (PROGRAM tablets) in cases with diagnosed concurrent gastrointestinal nematode infection. After elimination of the nematode infection confirmed by faecal examination, prevention of fleas should continue with PROGRAM tablets if indicated.

In puppies, treatment with Program Plus is recommended up to one month after weaning. Thereafter, prevention of fleas can be continued with lufenuron mono (Program).

Dogs travelling to a heartworm region:
To prevent flea infestations with concurrent heartworm prevention, dogs travelling to a heartworm risk region should begin medication within one month after arrival. Treatment should continue monthly, with the last administration given after the dog has left the region.

Dogs in a heartworm region:
To prevent flea infestations and to prevent heartworm, medication should begin within one month after the appearance of mosquitoes, or one month before the appearance of fleas, and continue throughout the risk period with the last dose given within one month after the mosquito and flea season finishes.

If dogs have a high level of flea infestation at the start of treatment, it may be necessary to apply a flea adulticide during the first one to two months. It is important to treat all dogs and cats in the household for fleas. Cats in the same household should be treated with PROGRAM oral or injectable suspension.

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

At 10x recommended dose rate (i.e. 5 mg milbemycin oxime, 100 mg lufenuron per kg) and higher dose rates clinical signs such as transient ataxia, trembling, depression, salivation, and mydriasis may be observed. There is no specific antidote.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Milbemycin oxime Anthelmintic, Lufenuron Insect Growth Regulator

ATC Vet Code: QP54AB51

5.1 Pharmacodynamic properties

Milbemycin belongs to the group of macrocyclic lactones, isolated from the fermentation of Streptomyces hygroscopicus var. aureolacrimosus. Out of the selected analogues, the one currently used for medicinal purposes is Milbemycin A3/A4 oxime (ratio □20 : □80). As one of the active principles in Program Plus, it is effective against larval stages (L3, L4, and the microfilariae) of Dirofilaria immitis, and anthelmintic activity against the following nematodes: *Toxocara canis*, *Trichuris vulpis*, *Ancylostoma caninum*. The activity of milbemycin is correlated with its action on invertebrate neurotransmission: it potentiates GABA (gamma-amino-butyric acid), an inhibitor of neuromuscular transmission, leading to paralysis.

Lufenuron belongs to the chemical group of benzoylureas, and is considered an IGR (Insect Growth Regulator) or IDI (Insect Development Inhibitor). It inhibits the development of fleas by interfering with the normal synthesis, polymerisation and deposition of the chitin, the principal component of the arthropod exoskeleton. The adult flea absorbs lufenuron via its bloodmeal. At therapeutic levels, lufenuron has no effect upon adult fleas, but passes transovarially to act upon certain stages of the development of the insect (egg and larva), thus interrupting the insect life cycle. Also, adult flea faeces containing lufenuron exert a larvicidal effect when ingested by the larvae directly.

5.2 Pharmacokinetic particulars

Milbemycin oxime is characterised by gastro-enteric absorption. It reaches peak plasma concentrations of about 200 - 300 ng/mL within about 2 to 5 hours after oral administration at recommended dose. Thereafter, milbemycin oxime concentrations decrease in plasma with a half life of about 1 to 3 days.

Following oral administration, lufenuron is distributed via the blood to the adipose tissue, from which, metabolically unmodified, it is constantly released above the minimum effective concentration for at least one month.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Titanium dioxide (E171)
Macrogol 8000
Cellulose, microcrystalline
Lactose monohydrate
Pregelatinised maize starch
Croscarmellose sodium
Hypromellose
Talc
Magnesium stearate

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the blister strips in the outer carton.

6.5 Nature and composition of immediate packaging

Carton containers, each containing 6 or 8 pentagonal tablets in PVDC/PVC blisters, thermosealed with aluminium foil, boxed in a free-opening, labelled carton.

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.

7. MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd
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8. MARKETING AUTHORISATION NUMBER

Vm 00879/4028

9. DATE OF FIRST AUTHORISATION

19 October 2000

10. DATE OF REVISION OF THE TEXT

September 2021

Approved 13 September 2021