SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FRONTPRO 136 mg chewable tablets for dogs >25–50 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substance:

FRONTPRO	Afoxolaner (mg)
chewable tablets for dogs >25–50 kg	136

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets.
Mottled red to reddish brown, rectangular shaped

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of flea infestation in dogs (*Ctenocephalides felis* and *C. canis*) One treatment provides immediate and persistent flea killing activity for 5 weeks. The product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD) where this has been previously diagnosed by a veterinarian.

Treatment of tick infestation in dogs (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus).* One treatment provides immediate and persistent tick killing activity for one month.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.

4.3 Contraindications

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

4.4 Special warnings for each target species

Unnecessary use of antiparasitics or use deviating from the instructions provided 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 infestation based on its epidemiological features, for each individual animal.

Parasites need to start feeding on the host to become exposed to afoxolaner; therefore the risk of the transmission of parasite borne diseases cannot be excluded.

When treating infestations of parasites, all in-contact animals should be treated with an appropriate product at the same time.

All stages of fleas can infest the dog's bedding and regular resting areas such as carpets and soft furnishings. In case of massive flea infestation and at the beginning of the control measures, these areas should be treated with a suitable environmental product and then vacuumed regularly.

Activity of the product is not affected if treated dogs are exposed to water.

4.5 Special precautions for use

Special precautions for use in animals

In the absence of available data, a veterinary surgeon should be consulted before treatment of puppies less than 8 weeks of age and/or dogs less than 2 kg bodyweight.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This product may be harmful following ingestion.
To prevent children from getting access to the veterinary medicinal product, remove only one chewable tablet at a time from the blister. Return the blister with the remaining chewable tablets into the carton.

Wash hands after handling the product.

Other precautions
The active substance is mostly excreted in the faeces (poo) and may be toxic to non-target organisms. To avoid contamination of the environment, ensure that dog faeces are bagged up and disposed of safely.

4.6 Adverse reactions (frequency and seriousness)

Mild gastrointestinal effects (vomiting, diarrhoea), pruritus, lethargy, anorexia, and neurological signs (convulsions, ataxia and muscle tremors) have been reported very rarely. Most reported adverse reactions were self-limiting and of short duration.

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 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Can be used in breeding, pregnant and lactating female dogs.
The safety of the veterinary medicinal product has not been established in breeding males.
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity of males.

Consult a veterinary surgeon before treatment of breeding males.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For oral use.

Dosage:
The product should be administered at a dose of 2.7–7 mg/kg bodyweight in accordance with the following table:

Bodyweight of dog (kg)	**Strength and number of chewable tablets to be administered**			
	FRONTPRO 11 mg	FRONTPRO 28 mg	FRONTPRO 68 mg	FRONTPRO 136 mg
2–4	1			
>4–10		1		
>10–25			1	
>25–50				1

For dogs above 50 kg bodyweight, use an appropriate combination of chewable tablets of different/same strengths. The tablets should not be divided.

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 before use.

Method of administration:
The tablets are chewable and palatable to most dogs. If the dog does not accept the tablets directly they may be administered with food.

Treatment schedule:
Treatment of flea and tick infestations:
For optimal control of flea and tick infestations, the product should be administered at monthly intervals throughout the flea and/or tick seasons, based on local epidemiological situations and the animal's lifestyle.

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

No adverse reactions were observed in healthy Beagle puppies over 8 weeks of age when treated with 5 times the maximum dose repeated 6 times at intervals of two to four weeks.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.
ATC vet code: QP53BE01.

5.1 Pharmacodynamic properties

Afoxolaner is an insecticide and acaricide belonging to the isoxazoline family. Afoxolaner acts at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. This results in uncontrolled activity of the central nervous system and death of insects or acarines. The selective toxicity of afoxolaner between insect/acarines and mammals may be inferred by the differential sensitivity of the insect/acarines' GABA receptors versus mammalian receptors.

Afoxolaner is active against adult fleas as well as several tick species such as *Dermacentor reticulatus* and *D. variabilis, Ixodes ricinus* and *I. scapularis, Rhipicephalus sanguineus, Amblyomma americanum* and *Haemaphysalis longicornis.*

FRONTPRO kills fleas within 8 hours and ticks within 48 hours.

The product kills fleas before egg production and therefore prevents household contamination.

5.2 Pharmacokinetic particulars

After oral administration in dogs, afoxolaner was shown to have high systemic absorption following administration. The absolute bioavailability was 74%. The mean maximum concentration (C_{max}) was 1,655 ± 332 ng/ml in plasma at 2–4 hours (T_{max}) after a 2.5 mg/kg afoxolaner dose.

Afoxolaner distributes into tissues with a volume of distribution of 2.6 ± 0.6 l/kg and a systemic clearance value of 5.0 ± 1.2 ml/hr/kg. The terminal plasma half-life is approximately 2 weeks in most dogs; however, half-life of afoxolaner can differ between dogs (e.g. in one study, $t_{½}$ in Collies at 25 mg/kg bodyweight was up to 47.7 days) with no effect on safety. *In-vitro* experiments demonstrated that P-glycoprotein efflux does not occur, confirming that afoxolaner is not a substrate for the P-glycoprotein transporters.
Afoxolaner in the dog is metabolised to more hydrophilic compounds and then eliminated. The metabolites and parent compound are eliminated from the body via urinary and biliary excretion with the majority eliminated in the bile. No evidence of enterohepatic recycling has been observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Soy protein fines
Braised beef flavouring
Povidone (E1201)
Macrogol 400
Macrogol 4000
Macrogol 15 hydroxystearate
Glycerol (E422)
Medium-chain triglycerides

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

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

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

The veterinary medicinal product is individually packaged in thermoformed laminated PVC blisters with paper-backed aluminium (Aclar/PVC/Alu).

One carton contains one blister of 1, 3 or 6 chewable 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

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

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim am Rhein
Germany

8. MARKETING AUTHORISATION NUMBER

Vm 04491/5010

9. DATE OF FIRST AUTHORISATION

20 May 2019

10. DATE OF REVISION OF THE TEXT

November 2024

Approved 18 November 2024
Gavin Hall