SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fiproxile 268 mg/2400 mg spot-on solution for large dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4.4 ml pipette contains:

Active substances:
Fipronil 268.4 mg
Permethrin 2398.0 mg

Excipients:
Butylhydroxyanisole (E320) 0.88 mg
Butylhydroxytoluene (E321) 0.44 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on solution.
Clear yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

In dogs, to be used against infestations with fleas and/or ticks when repellent (anti-feeding) activity is also necessary against sand-flies and/or mosquitoes.

Fleas:
Treatment and prevention of infestations by fleas *(Ctenocephalides felis).* Fleas on dogs are killed within 24 hours following treatment. One treatment provides persistent efficacy against new infestations with adult fleas for four weeks. The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD) where this condition has previously been diagnosed by a veterinarian.

Ticks:
Treatment of infestations with *Ixodes ricinus* ticks.
One application provides four weeks persistent acaricidal efficacy against tick infestations (*Ixodes ricinus*, *Dermacentor reticulatus* and *Rhipicephalus sanguineus*).
If ticks of some species (*Dermacentor reticulatus* or *Rhipicephalus sanguineus*) are present at the time of application, not all ticks may be killed within 48 hours.

Sand-flies and mosquitoes:

One treatment provides repellent (anti-feeding) activity against sand-flies (*Phlebotomus perniciosus*) and against mosquitoes (*Culex pipiens, Aedes aegypti*) for four weeks.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Do not use on rabbits and cats as adverse reactions and even death can occur (see also section 4.5i).
Do not use on sick (e.g. systemic diseases, fever…) or convalescent animals.

4.4 Special warnings for each target species

The veterinary medicinal product remains effective after exposure to sunlight or if the animal becomes wet after rain.
Avoid frequent swimming or shampooing of treated dogs as this may adversely affect maintenance of product effectiveness.

A dog with fleas may show an allergic reaction to the flea saliva called Flea Allergy Dermatitis (FAD). If your dog has inflamed skin, is itchy and bites, scratches excessively and is restless and uncomfortable, you should seek the advice of a veterinarian to diagnose if your dog suffers from FAD.

To reduce re-infestation from emergence of new fleas, it is recommended to treat all dogs in a household. Other animals living in the same household should also be treated with a suitable product. Fleas from pets often infest the animal's basket, bedding and regular resting areas such as carpets and soft furnishings which should be treated, in case of massive infestation and at the beginning of the control measures, with a suitable insecticide and vacuumed regularly.

There may be an attachment of single ticks or bites by single sand-flies or mosquitoes. For this reason, the transmission of infectious diseases by these parasites cannot be excluded if conditions are unfavourable.

Studies have shown anti-feeding effect of four weeks for sand-flies and mosquitoes. Therefore, for short-term travel (less than 4 weeks) to endemic areas it is recommended to apply the treatment immediately before expected exposure. For longer-term exposure (e.g. animals living in endemic areas or travel duration longer than 4 weeks), the treatment schedule should be based on local epidemiological information.

4.5 Special precautions for use

<u>i) Special precautions for use in animals</u>
Animals should be weighed accurately prior to treatment.
The safety of the product has not been established in dogs younger than 12 weeks of age or in dogs weighing less than 1.5 kg.
Care should be taken to avoid the content of the pipette coming into contact with the eyes or mouth of the recipient dogs. In particular oral uptake due to the licking of the application site by treated or in-contact animals should be avoided.
This product is extremely poisonous to cats and could be fatal due to the unique physiology of cats which is unable to metabolise certain compounds including permethrin. In case of accidental dermal exposure, wash the cat with shampoo or soap, and seek veterinary advice rapidly. To prevent cats from being accidentally exposed to the product,

keep treated dogs away from cats after treatment until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog, which has been treated with this product. In case of exposure of this type, seek veterinary advice immediately if this occurs.
Do not use on rabbits and cats.

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

The product may cause neurotoxicity. The product may be harmful if swallowed. Avoid ingestion including hand-to-mouth contact. In the event of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
This product can cause eye and mucous membrane irritation. Therefore, avoid contact between the product and the mouth or eyes including hand-to-mouth and hand-to-eye contacts. In the event of accidental contact between the product and eyes, immediately and thoroughly flush the eyes with water. If eye irritation persists, seek medical advice and show the package leaflet or the label to the physician.
Avoid contact with the skin. Should the product come into contact with skin, wash the contacted area immediately with soap and water.
Wash hands thoroughly after use.
Do not eat, drink or smoke while handling the veterinary medicinal product.
People with a known hypersensitivity (allergy) to fipronil, permethrin or any of the other ingredients should avoid contact with the veterinary medicinal product, which, on very rare occasions, can cause respiratory irritation and dermal reactions in certain individuals.
Should symptoms occur, seek medical advice immediately and show the leaflet or the label to the physician.
Treated animals should not be handled or played with until the application site is dry and for about 12 hours after treatment. It is therefore recommended to treat the animals in the early evening or late afternoon in order to minimise contact with the treated animal. On the day of treatment, treated animals should not be permitted to sleep with their owner, especially children.
Keep the stored pipettes in the original packaging. In order to prevent children from getting access to used pipettes, dispose of used pipettes immediately in a proper way.

iii) Other precautions

Fipronil and permethrin may adversely affect aquatic organisms. Dogs should not be allowed to swim in water courses for 2 days after application.
The product may have adverse effects on painted, varnished or other household surfaces or furnishings. Allow the application site to dry before permitting contact with such materials.

4.6 Adverse reactions (frequency and seriousness)

Transient cutaneous reactions at the application site (pruritus, erythema, alopecia) and general pruritus have been reported very rarely. Behavioral changes (hyperactivity/agitation), neurological disorders (lethargy, muscle tremor, convulsions, ataxia) and vomiting have been reported very rarely.
If licking occurs, transient hypersalivation may be observed.

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

Laboratory studies in dogs using fipronil and permethrin have not shown any evidence of teratogenic or embryotoxic effect. The safety of the veterinary medicinal product has not been established during pregnancy and lactation in bitches. Use in pregnancy and lactation only in accordance with professional veterinary advice and a benefit/risk assessment.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

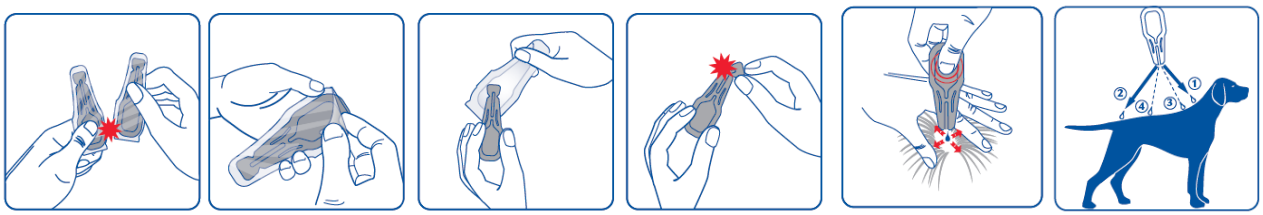
For external use only.
Spot-on use.

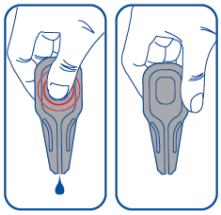
Dosage:
The recommended minimum dose is 6.7 mg fipronil /kg b.w.and 60 mg permethrin/kg b.w.

Dog weight	Fipronil (mg)	Permethrin (mg)
1.5-4 kg	26.8	240
4-10 kg	67	600
10-20 kg	134	1200
20-40 kg	268	2400
40-60 kg	402	3600

For dogs > 60 kg the appropriate combination of pipettes should be used.

Method of administration:
Remove the pipette from the overblister. Hold the pipette upright. Tap the narrow part of the pipette to ensure that the contents are within the main body of the pipette. Break the snap-off top of the spot-on pipette along the scored line.
Part the pet's coat until its skin is visible. Place the tip of the pipette directly against the bared skin and squeeze gently several times to empty its contents at two to four different points, depending on body weight, along the pet's back from the shoulder to the base of the tail.
As a guide, dogs under 20 kg should have the product applied in two spots, whereas those over 20 kg should receive the product in 2-4 spots.





Drop stop system.

Treatment schedule:

The use of the product should be based on a confirmed infestation or risk of infestation, with fleas and/or ticks when repellent (anti-feeding) activity is also necessary against sand-flies and/or mosquitoes.

Depending on the ectoparasite challenge the responsible veterinary surgeon may recommend repeating the treatment. The interval between two treatments should be at least 4 weeks.

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

Safety has been demonstrated with up to 5 times the maximum recommended dose in healthy 12-week old puppies treated 3 times at intervals of 3 weeks.

The risk of experiencing adverse reactions (see section 4.6) may however increase with overdosing, so animals should always be treated with correct pipette size according to bodyweight.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for topical use, permethrin, combinations
ATCvet code: QP53AC54

The product is an ectoparasiticide for topical use containing fipronil and permethrin. This combination acts as an insecticide, acaricide and as a repellent to sand-flies and mosquitoes.

5.1 Pharmacodynamic properties

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family. Fipronil and its metabolite fipronil sulfone act at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA) as well as desensitising (D) and non-desensitising (N) channels gated by glutamate (Glu, unique invertebrate ligand-gated chloride channels), 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 acari.

Permethrin belongs to the type I class of pyrethroid acaricides and insecticides and also acts as repellent. Pyrethroids affect the voltage-gated sodium channels in vertebrates and non-vertebrates. Pyrethroids are so called “open channel blockers” affecting the sodium channel by slowing both the activation and the inactivation properties thus leading to hyperexcitability and death of the parasite.

The product provides an immediate and persistent insecticidal activity against fleas (*Ctenocephalides felis*), immediate acaricidal activity against *Ixodes ricinus* ticks, persistent acaricidal activity against ticks (*Rhipicephalus sanguineus*, *Dermacentor reticulatus* and *Ixodes ricinus*) and repellent (anti-feeding) activity against sand-flies (*Phlebotomus perniciosus*) and mosquitoes (*Culex pipiens, Aedes aegypti*).

When applied to dogs at least 2 days prior to tick exposure, the product was experimentally shown to indirectly reduce the risk of *Babesia canis canis* transmission from infected ticks *Dermacentor reticulatus* until 28 days after application, thereby reducing the risk of canine babesiosis in treated dogs.

5.2 Pharmacokinetic particulars

The major metabolite of Fipronil is the sulfone derivative, which also possesses insecticidal and acaricidal properties.
Following topical application to dogs, under the normal conditions of use:
- Permethrin and fipronil, together with its major metabolite, are well distributed in the haircoat of the dog within one day after application. The concentrations of fipronil, fipronil sulfone and permethrin in the haircoat coat decrease with time and are detectable for at least 35 days after application.
- Fipronil plasma concentrations peak after 5 days whereas its active metabolite peaks around 14 days. Concentrations are quantifiable up to 35 days. Permethrin displays very low levels of systemic absorption.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxyanisole (E320)
Butylhydroxytoluene (E321)
Benzyl alcohol (E1519)
Diethylene glycol monoethyl ether

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: immediate use.

6.4 Special precautions for storage

Store below 30°C.

Keep the blister pack in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Transparent multi-layer plastic single-dose pipettes containing 4.40 ml obtained by thermoforming a transparent bottom complex (polyacrylonitrile-methacrylate or polyethylene-ethylene vinyl alcohol-polyethylene/polypropylene/cyclic olefin copolymer/polypropylene) and closed by heat sealing with a lid complex (polyacrylonitrile-methacrylate or polyethylene-ethylene vinyl alcohol-polyethylene/aluminium/polyethylene-terephthalate).

The boxes contain individual pipette(s) placed in coloured overblister(s) made from polypropylene/cyclic olefin copolymer/polypropylene and closed with lid made from polyethylene-terephthalate/aluminium/polypropylene.

Boxes of 1, 2, 4 or 6 pipettes.

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.
Do not contaminate ponds, waterways or ditches with the veterinary medicinal product or empty container as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Alfamed
13ème Rue - L.I.D.
06517 Carros Cedex
France

8. MARKETING AUTHORISATION NUMBER

Vm 17902/4073

9. DATE OF FIRST AUTHORISATION

03 July 2014

10. DATE OF REVISION OF THE TEXT

August 2019

Approved: 14 August 2019