

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fipronil-(S)-Methoprene Ceva Spot-on Solution for Dogs 40-60 kg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4.24 ml pipette contains:

Active substances:

Fipronil	720.80 mg
(S)-methoprene	360.4 mg

Excipients:

Butylhydroxyanisole E320	0.848 mg
Butylhydroxytoluene E321	0.848 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 40-60 kg

4.2 Indications for use, specifying the target species

- Treatment and prevention of flea and/or tick infestations.
- Treatment and prevention of flea infestations (*Ctenocephalides* spp.). Immediate insecticidal efficacy against new infestations with adult fleas persists for 9 weeks. Prevention of the multiplication of fleas by inhibiting the hatching of flea eggs (ovicidal activity) and the development of flea eggs into adult fleas for 8 weeks after application.
- Treatment and prevention of tick infestation (*Dermacentor reticulatus*, *Rhipicephalus sanguineus*). The product has immediate and persistent acaricidal efficacy for 6 weeks after application.

The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

4.3 Contraindications

Do not use on rabbits, as adverse reactions even mortality could occur.

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

Do not use on sick (e.g. systemic disease, fever) or convalescent animals.

This product is specifically developed for dogs. Do not use in cats, as this could lead to overdosing.

4.4 Special warnings for each target species

All stages of fleas can infest the dog's basket, bedding, and regular resting areas such as carpets and soft furnishings. In cases of massive flea infestation and at the beginning of the control measures these areas should be treated with a suitable environmental product. To reduce environmental flea challenge, all animals living in the same household should also be treated with a suitable flea control product.

For the treatment and control of flea allergy dermatitis it is recommended that allergic patients and all other animals in the household should be treated on a regular basis.

The effect of bathing dogs on the duration of product efficacy against fleas has been studied.

Weekly water immersion of dogs following treatment had no effect on the duration of efficacy. Shampooing of dogs with an emollient shampoo 48 hours prior to treatment had no effect on duration of efficacy. Weekly shampooing with an emollient shampoo in dogs may reduce the duration of efficacy to 3 weeks against adult fleas and to 6 weeks against immature stages of fleas. Weekly bathing with a chlorhexidene shampoo may reduce effectiveness against adult fleas to 3 weeks.

4.5 Special precautions for use

Special precautions for use in animals

The attachment of single ticks after treatment cannot be ruled out. Therefore the transmission of infectious disease cannot be completely excluded if conditions are unfavourable.

For external use only. Do not administer orally.

Avoid contact with the eyes of the animal. If the product is in contact with eyes, rinse immediately with plenty of water.

Do not apply the product on wounds or skin lesions.

Wait for the application site to dry before allowing the treated dog to come into contact with valuable fabrics or furnishings. It is important to make sure that the veterinary medicinal product is applied directly onto an area of dry skin where the animal cannot lick it off and to make sure that animals do not lick each other following treatment.

In the absence of additional safety studies, do not repeat the treatment at intervals of less than 2 weeks.

The safety of the product has not been established in dogs younger than 8 weeks of age weighing less than 2 kg bodyweight (bw).

Use only according to the benefit/risk assessment by the responsible veterinarian.

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

This product can cause mucous membrane, skin and eye irritation.

Avoid contact of the product with skin, eyes or mouth.

People with known hypersensitivity to fipronil or s-methoprene and/or any of the ingredients should avoid contact with the veterinary medicinal product.

Treated animals should not be handled or played with for at least 12-hours after treatment. Animals should be treated in the evening 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.

Do not eat, drink or smoke while handling the product.

Wash hands thoroughly after use.

In case of accidental spillage on skin, wash off immediately with soap and water.

If the product accidentally gets into the eyes, they should be thoroughly flushed with water.

If the product is accidentally swallowed, seek medical advice immediately and show the package leaflet to the physician.

Keep stored pipettes in the original packaging until ready to use. In order to prevent children from getting access to used pipettes, dispose of used pipettes immediately.

Other precautions

Treated dogs should not be allowed to swim in watercourses for 48 hours after application of the product.

4.6 Adverse reactions (frequency and seriousness)

Transient cosmetic effects at the application site such as spiking of the hair, wet appearance, dry residue or slight scaling were very rarely observed in spontaneous reports. These changes do not affect the safety or the efficacy of the product.

Transient hypersalivation (mainly due to the excipients of the product) after licking the product and vomiting after swallowing were observed very rarely in spontaneous reports.

Alopecia and pruritus at application site have been reported very rarely based on post marketing safety experience.

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 have not produced any evidence of teratogenic or fetotoxic effects with fipronil, although developmental effects (e.g. neurotoxicity) have been shown in rats in one study.

The safety of the veterinary medicinal product has not been established in dogs during pregnancy and lactation. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Spot-on use.
Dogs 40-60 kg

One pipette per animal corresponding to the minimal recommended dose of 12 mg/kg bw of fipronil and 6 mg/kg bw of (S)-methoprene.

How to apply:

Disconnect one of the blisters from the card. This helps to avoid accidental opening of the adjacent blister in order to protect the still unopened pipettes from exposure to humidity. Open the blister with scissors. To avoid damaging the pipette cut along the line marked with the scissors icon. Carefully peel back the foil from the cut off end and withdraw the pipette.



Hold the pipette upright. Tap lightly to ensure the entire liquid content is within the main body of the pipette. Bend the upper border strip backwards. Then the pipette can be set aside, if necessary. To open the pipette, snap off the top of the pipette along the scored line.



Part the coat between the shoulder blades until the skin is visible. Place the tip of the pipette on the skin and squeeze the pipette several times to empty its content completely and directly onto the skin in one spot.



Application of the solution near the base of the neck minimises the possibility that the animal will lick the solution off. Care should be taken after the application that animals do not mutually lick off the solution.

Care should be taken to avoid excessive wetting of the hair with the product since this will cause a sticky appearance of hairs at the treatment spot.

Treatment can be repeated every 6 weeks or as considered appropriate for the type and level of parasitic exposure. In the absence of appropriate studies, the treatment should not be repeated at intervals of less than 2 weeks.

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

No adverse effects were observed in a target animal safety study conducted in 8 weeks old puppies weighing approximately 2 kg bw treated on 7 consecutive occasions at 2 weeks intervals with up to 5x the recommended dose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for topical use, fipronil combinations.
ATCvet code: QP53AX65

The product is an insecticidal and acaricidal solution for topical use, containing an association of an adulticidal active ingredient, fipronil, in combination with an ovicidal and larvicidal active ingredient, (S)-methoprene.

5.1 Pharmacodynamic properties

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family. It acts by interacting with 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 arthropods such as fleas and ticks. Fipronil acts by contact. After topical administration, fipronil accumulates itself in sebaceous glands and is released progressively on hair surface via follicular ducts. Fipronil usually kills fleas within 24 hours and ticks within 48 hours.

(S)-methoprene is an insect growth regulator (IGR) of the class of compounds known as juvenile hormone analogues that inhibit the development of immature stages of insects. This compound mimics the action of juvenile hormone and causes impaired development and death of the developing stages of fleas. (S)-methoprene acts by contact. The on-animal ovicidal activity of (S)-methoprene results from either inhibition of egg laying by absorption through the cuticle of the adult fleas or from inhibition of egg hatching by direct penetration in newly laid eggs. In the environment of the treated animal, (S)-methoprene is also effective in the elimination of flea larvae and pupae, preventing these stages from developing into adults. This prevents further contamination with newly emerged adult fleas.

5.2 Pharmacokinetic particulars

Fipronil

Fipronil is poorly absorbed through the skin. After topical application in clinical conditions (licking not prevented), peak fipronil plasma concentrations (mean C_{max} 25.5 ng/ml) are slowly attained (mean t_{max} approximately 96 h). Fipronil is metabolized to fipronil sulfone.

Fipronil and its major metabolite are well-distributed in the haircoat after topical administration.

(S)-methoprene

Plasma concentrations of S-methoprene were generally below the limit of quantification (10 ng/mL) after topical application.

5.3 Environmental properties

The product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxyanisole (E320).
Butylhydroxytoluene (E321).
Ethanol (anhydrous).
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.

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 pipettes are made of:

Front foil:	Polypropylene / polyethylene terephthalate
Lidding foil:	Polyester /aluminium / polyester / polyethylene terephthalate

Pipettes are packed in child resistant blisters.

Cardboard box of 1, 3, 6, 12, 24, 60 or 120 pipettes of 4.24 ml.

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 products 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

Ceva Sante Animale
10, av. de La Ballastiere
33500 Libourne
France

8. MARKETING AUTHORISATION NUMBER

Vm 14966/4016

9. DATE OF FIRST AUTHORISATION

24 August 2015

10. DATE OF REVISION OF THE TEXT

July 2020

A handwritten signature in black ink, consisting of several loops and a long horizontal stroke extending to the right.

Approved 15 July 2020