A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box containing 1, 3, 6, 12, 24, 60 or 120 pipettes

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 10-20 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 20-40 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 40-60 kg

Fipronil / (S)-methoprene

2. STATEMENT OF ACTIVE SUBSTANCES

Each pipette delivers 239.70 mg of fipronil and 119.85 mg of (S)-methoprene
Each pipette delivers 479.4 mg of fipronil and 239.70 mg of (S)-methoprene
Each pipette delivers 720.80 mg of fipronil and 360.4 mg of (S)-methoprene

3. PHARMACEUTICAL FORM

Spot-on solution.

4. PACKAGE SIZE

1 pipette (1.41 ml, 2.82 ml, 4.24 ml)
3 pipettes (1.41 ml, 2.82 ml, 4.24 ml)
6 pipettes (1.41 ml, 2.82 ml, 4.24 ml)
12 pipettes (1.41 ml, 2.82 ml, 4.24 ml)
24 pipettes (1.41 ml, 2.82 ml, 4.24 ml)
60 pipettes (1.41 ml, 2.82 ml, 4.24 ml)
120 pipettes (1.41 ml, 2.82 ml, 4.24 ml)

5. TARGET SPECIES

Dogs 10-20 kg
Dogs 20-40 kg
Dogs 40-60 kg

6. INDICATION(S)

Treats and prevents tick and flea infestations.
Controls all flea stages (adults, eggs, larvae and pupae).

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For external use only.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read Package Leaflet for user warnings before using the product.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

16. MARKETING AUTHORISATION NUMBER(S)

Vm 14966/4014

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fipronil-(S)-Methoprene Ceva
Spot-on

10-20 kg
20-40 kg
40-60 kg

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

1.41 ml
2.82 ml
4.24 ml

4. ROUTE(S) OF ADMINISTRATION

Spot-on

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot:

7. EXPIRY DATE

EXP:

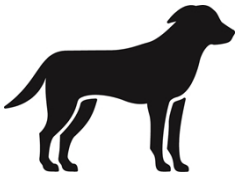
8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fipronil-(S)-Methoprene Ceva
Spot-on



10-20 kg
20-40 kg
40-60 kg

Fipronil 239.70 mg / (S)-methoprene 119.85 mg
Fipronil 479.4 mg / (S)-methoprene 239.7 mg
Fipronil 720.80 mg / (S)-methoprene 360.4 mg

2. NAME OF THE MARKETING AUTHORISATION HOLDER

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 10-20 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 20-40 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 40-60 kg

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

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

Manufacturers responsible for batch release:

Ceva Santé Animale
10, av. de La Ballastière
33500 Libourne
France

Klocke Verpackungs-Service GmbH
Max-Becker-Str. 6
76356 Weingarten
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 10-20 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 20-40 kg
Fipronil-(S)-Methoprene Ceva spot-on solution for dogs 40-60 kg
Fipronil, (S)-methoprene

3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS

Each pipette contains:

		Active substances		Excipients	
	Volume of unit dose (ml)	Fipronil (mg)	(S)-methoprene (mg)	Butylhydro-xyanisole E320 (mg)	Butylhydro-xytoluene E321 (mg)
Dogs 10-20 kg	1.41	239.70	119.85	0.282	0.282
Dogs 20-40 kg	2.82	479.4	239.70	0.564	0.564
Dogs 40-60 kg	4.24	720.80	360.4	0.848	0.848

Clear yellow solution.

4. INDICATIONS

Treatment and prevention of flea and/or tick infestations.
The product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD).

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 acaricidal efficacy and persistent acaricidal efficacy for 6 weeks after application.

5. 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.

6. ADVERSE REACTIONS

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)

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs 10-20 kg - Dogs 20-40 kg - Dogs 40-60 kg

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

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

Route
Spot-on use.
Dogs 10-20 kg - Dogs 20-40 kg - Dogs 40-60 kg

Administration
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 peal 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.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

11. SPECIAL STORAGE PRECAUTIONS

Keep out the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use after the expiry date which is stated on the pipette and on the carton after EXP. The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

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 animals. 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 animal to come into contact with valuable fabrics or furnishings.
It is important to make sure that the 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 animals younger than 8 weeks of age. It has not been evaluated in dogs < 2 kg 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 skin or if eye irritation persists, or 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:
All stages of fleas can infest the animal'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.
Treated dogs should not be allowed to swim in watercourses for 48 hours after application of the product.

Pregnancy and lactation:
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.

Overdose (symptoms, emergency procedures, antidotes):
No adverse effects were observed in a target animal safety studies conducted in 8 weeks old puppies weighing **≥** 2 kg bw treated on 7 consecutive occasions at 2 week intervals with up to 5x the recommended dose.

Interaction with other medicinal products and other forms of interaction:
None known.

Incompatibilities:
Not applicable.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

June 2020

15. OTHER INFORMATION

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.

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 of dogs after topical administration.

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

Pack sizes:
Dogs 10-20 kg: Cardboard box of 1, 3, 6, 12, 24, 60 or 120 pipettes of 1.41 ml.
Dogs 20-40 kg: Cardboard box of 1, 3, 6, 12, 24, 60 or 120 pipettes of 2.82 ml.
Dogs 40-60 kg: Cardboard box of 1, 3, 6, 12, 24, 60 or 120 pipettes of 4.24 ml.
Not all pack sizes may be marketed.
Pipettes are packed in child resistant blisters.

Approved July 2020