1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 112.5 mg spot-on solution for very small dogs (2 – 4.5 kg)
Bravecto 250 mg spot-on solution for small dogs (>4.5 – 10 kg)
Bravecto 500 mg spot-on solution for medium-sized dogs (>10 – 20 kg)
Bravecto 1 000 mg spot-on solution for large dogs (>20 – 40 kg)
Bravecto 1 400 mg spot-on solution for very large dogs (>40 – 56 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each ml contains 280 mg fluralaner.
Each pipette delivers:

Bravecto spot-on solution	**Pipette content (ml)**	**Fluralaner (mg)**
for very small dogs 2 – 4.5 kg	0.4	112.5
for small dogs >4.5 – 10 kg	0.89	250
for medium-sized dogs >10 – 20 kg	1.79	500
for large dogs >20 – 40 kg	3.57	1 000
for very large dogs >40 – 56 kg	5.0	1 400

Excipients:

Qualitative composition of excipients and other constituents
Dimethylacetamide
Glycofurol
Diethyltoluamide
Acetone

Clear colourless to yellow spot-on solution.

3. CLINICAL INFORMATION

3.1 Target species

Dog

3.2 Indications for use for each target species

For the treatment of tick and flea infestations in dogs.

This veterinary medicinal product is a systemic insecticide and acaricide that provides:
- immediate and persistent flea (*Ctenocephalides felis* and *Ctenocephalides canis*) killing activity for 12 weeks, and
- immediate and persistent tick (*Ixodes ricinus, Rhipicephalus sanguineus* and *Dermacentor reticulatus*) killing activity for 12 weeks.

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

The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For the treatment of demodicosis caused by *Demodex canis*.

For the treatment of sarcoptic mange (*Sarcoptes scabiei* var. *canis*) infestation.

3.3 Contraindications

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

3.4 Special warnings

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

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the veterinary medicinal 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.

The possibility that other animals in the same household can be a source of re-infection with parasites should be considered, and these should be treated as necessary with an appropriate veterinary medicinal product.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Care should be taken to avoid contact with the eyes of the animal.
Do not use directly on skin lesions.
Do not wash or allow the dog to become immersed in water or swim in water courses within 3 days after treatment.
In the absence of available data, this veterinary medicinal product should not be used on puppies less than 8 weeks old and /or dogs weighing less than 2 kg.
The veterinary medicinal product should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
This veterinary medicinal product is for topical use and should not be administered orally.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Contact with the veterinary medicinal product should be avoided and disposable protective gloves obtained with this veterinary medicinal product at the point of sale must be worn when handling the veterinary medicinal product for the following reasons:
Hypersensitivity reactions have been reported in a small number of people, which can potentially be serious.
Persons with a hypersensitivity to fluralaner or to any of the excipients should avoid any exposure to the veterinary medicinal product.
The veterinary medicinal product binds to skin and may also bind to surfaces after spillage of the veterinary medicinal product. Skin rashes, tingling or numbness have been reported in a small number of individuals after skin contact.
If skin contact does occur, wash the affected area immediately with soap and water. In some cases, soap and water are not sufficient to remove the veterinary medicinal product spilled on the fingers.
Contact with the veterinary medicinal product may also occur when handling the treated animal. Make sure that your animal's application site is no longer noticeable before resuming contact with the site of application. This includes cuddling the animal and sharing a bed with the animal. It takes up to 48 hours for the application site to become dry but it will be noticeable for longer.
If skin reactions occur, consult a physician and show them the veterinary medicinal product packaging.
People with a sensitive skin or known allergy in general e.g. to other veterinary medicinal products of this type should handle the veterinary medicinal product as well as treated animals with caution.
This veterinary medicinal product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.

This veterinary medicinal product is harmful after ingestion. Keep the veterinary medicinal product in the original packaging until use, in order to prevent children from getting direct access to the veterinary medicinal product. A used pipette should immediately be disposed of. In case of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician.
The veterinary medicinal product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.In case of spillage onto, for example table or floor surfaces, remove excess veterinary medicinal product using paper tissue and clean the area with detergent.

Special precautions for the protection of the environment:
Treated dogs should not be allowed to enter surface water for 48 hours after treatment to avoid adverse effects on aquatic organisms.

3.6 Adverse events

Dog:

Common (1 to 10 animals / 100 animals treated):	Skin reactions at the application site (such as Erythema, Alopecia) [#]
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Lethargy, Anorexia; Emesis, Diarrhoea; Pruritus; Muscle tremor, Ataxia, Convulsion.

[#] mild and transient

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See also section ´Contact details´ of the package leaflet.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product in breeding, pregnant and lactating dogs has been demonstrated. Can be used in breeding, pregnant and lactating dogs.

3.8 Interaction with other medicinal products and other forms of interaction

None known.
Fluralaner is highly bound to plasma proteins and might compete with other highly bound active substances such as non-steroidal anti-inflammatory drugs (NSAIDs) and the coumarin derivative warfarin. Incubation of fluralaner in the presence of carprofen or warfarin in dog plasma at maximum expected plasma concentrations did not reduce the protein binding of fluralaner, carprofen or warfarin. During laboratory and clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products were observed.

3.9 Administration routes and dosage

For spot-on use.

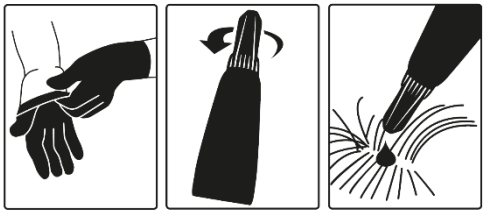
The veterinary medicinal product should be administered in accordance with the following table (corresponding to a dose of 25 - 56 mg fluralaner/kg body weight):

Body weight of dog (kg)	Strength and number of pipettes to be administered				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1 000 mg	Bravecto 1 400 mg
2 - 4.5	1				
>4.5 - 10		1			
>10 - 20			1		
>20 - 40				1	
>40 - 56					1

For dogs above 56 kg body weight, use a combination of two pipettes that most closely matches the body weight.
Underdosing could result in ineffective use and may favour resistance development.

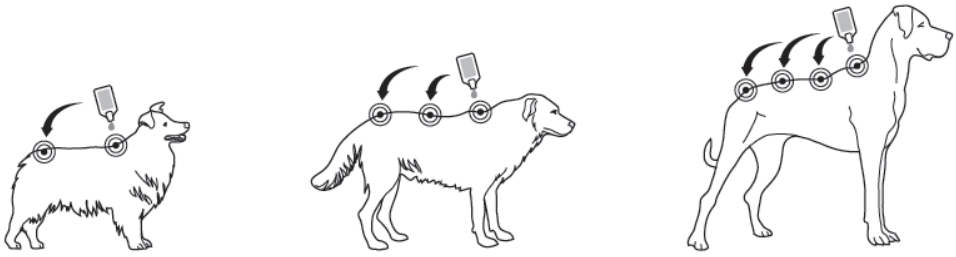
Method of administration

Step 1: Immediately before use, open the sachet and remove the pipette. Put on gloves. The pipette should be held by the base or by the upper rigid portion below the cap in an upright position (tip up) for opening it. The cap should be rotated clockwise or counter clockwise one full turn. The cap will stay on the pipette; it is not possible to remove it. The pipette is open and ready for application when the breaking of the seal is felt.



Step 2: The dog should be standing or lying with its back horizontal during application. Place the pipette tip vertically against the skin between the shoulder blades of the dog.

Step 3: Squeeze the pipette gently and apply the entire contents directly to the dog's skin in one (when volume is small) or several spots along the dog's dorsal line from the shoulder to the base of the tail. Avoid the application of more than 1 ml of solution at any one spot as it could cause some of the solution to run or drip off the dog.



Treatment schedule

For infestations with fleas and ticks, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.
For optimal control of tick and flea infestation, the veterinary medicinal product should be administered at intervals of 12 weeks.
For the treatment of *Demodex canis* mite infestations, a single dose of the veterinary medicinal product should be applied. As demodicosis is a multi-factorial disease, it is advisable to also treat any underlying disease appropriately.
For the treatment of sarcoptic mange infestations (*Sarcoptes scabiei* var. *canis*), a single dose of the veterinary medicinal product should be applied. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No adverse reactions were observed following topical administration to puppies aged 8 – 9 weeks and weighing 2.0 – 3.7 kg treated with overdoses of up to 5 times the maximum recommended dose (56 mg, 168 mg and 280 mg fluralaner/kg body weight) on three occasions at shorter intervals than recommended (8-week intervals).

There were no findings on reproductive performance and no findings of concern on offspring viability when fluralaner was administered orally to Beagle dogs at overdoses of up to 3 times the maximum recommended dose (up to 168 mg/kg body weight of fluralaner).

Fluralaner was well tolerated in Collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the maximum recommended dose (168 mg/kg body weight). No treatment-related clinical signs were observed.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP53B E02.

4.2 Pharmacodynamics

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp*., Dermacentor* spp. and *Rhipicephalus sanguineus*), fleas (*Ctenocephalides* spp.), *Demodex canis* mites and sarcoptic mange (*Sarcoptes scabiei* var*. canis*) on the dog.

The onset of efficacy is within 8 hours for fleas (*C. felis*) and 12 hours for ticks (*I. ricinus*).

Fluralaner has a high potency against ticks and fleas by exposure via feeding, i.e. it is systemically active on target parasites.

Fluralaner is a potent inhibitor of parts of the arthropod nervous system by acting antagonistically on ligand-gated chloride channels (GABA-receptor and glutamate-receptor).

In molecular on-target studies on insect GABA receptors of flea and fly, fluralaner is not affected by dieldrin resistance.

In *in vitro* bio-assays, fluralaner is not affected by proven field resistances against amidines (tick), organophosphates (tick, mite), cyclodienes (tick, flea, fly), macrocyclic lactones (sea lice), phenylpyrazoles (tick, flea), benzophenyl ureas (tick), pyrethroids (tick, mite) and carbamates (mite).

The veterinary medicinal product contributes towards the control of the environmental flea populations in areas to which treated dogs have access.

Newly emerged fleas on a dog are killed before viable eggs are produced. An *in vitro* study also demonstrated that very low concentrations of fluralaner stop the production of viable eggs by fleas. The flea life cycle is broken due to the rapid onset of action and long-lasting efficacy against adult fleas on the animal and the absence of viable egg production.

4.3 Pharmacokinetics

Fluralaner is readily absorbed from the topical administration site into the hair, skin and subjacent tissues, from where it is slowly absorbed into the vascular system. A plateau is seen in plasma between 7 and 63 days post administration, after which concentrations decline slowly. The prolonged persistence and slow elimination from plasma ($t_{1/2}$ = 21 days) and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval. Unchanged fluralaner is excreted in feces and to a very low extent in urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
Bravecto 112.5 mg spot-on solution: 2 years
Bravecto 250 mg / 500 mg / 1 000 mg / 1 400 mg spot-on solution: 3 years

5.3 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions. The pipettes should be kept in the outer packaging to prevent solvent loss or moisture uptake. The sachets should only be opened immediately prior to use.

5.4 Nature and composition of immediate packaging

Unit dose pipette made of laminated aluminium/polypropylene foil closed with an HDPE cap and packed in a laminated aluminium foil sachet. Each carton box contains 1 or 2 pipettes and a pair of gloves per pipette.
Not all pack sizes may be marketed.

5.5 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 or household waste.
The veterinary medicinal product should not enter water courses as fluralaner may be dangerous for aquatic invertebrates.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/158/016-017	112.5 mg
EU/2/13/158/020-021	250 mg
EU/2/13/158/024-025	500 mg
EU/2/13/158/028-029	1 000 mg

EU/2/13/158/030-031 1 400 mg

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 11/02/2014

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).