ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each chewable tablet contains:

Bravecto chewable tablets	**Fluralaner (mg)**
for very small dogs (2 – 4.5 kg)	112.5
for small dogs (>4.5 – 10 kg)	250
for medium-sized dogs (>10 – 20 kg)	500
for large dogs (>20 – 40 kg)	1 000
for very large dogs (>40 – 56 kg)	1 400

Excipients:

Qualitative composition of excipients and other constituents
Pork liver flavour
Sucrose
Maize starch
Sodium lauryl sulfate
Disodium pamoate monohydrate
Magnesium stearate
Aspartame
Glycerol
Soya-bean oil
Macrogol 3350

Light to dark brown chewable tablet with a smooth or slightly rough surface and circular shape. Some marbling, speckles or both may be visible.

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*) killing activity for 12 weeks,

- immediate and persistent tick killing activity for 12 weeks for *Ixodes ricinus, Dermacentor reticulatus* and *D. variabilis,*
- immediate and persistent tick killing activity for 8 weeks for *Rhipicephalus sanguineus,*
- persistent tick killing activity from 7 days to 12 weeks after treatment for *Ixodes hexagonus.*

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.

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for up to 12 weeks. The effect is indirect due to the veterinary medicinal product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for up to 12 weeks. The effect is indirect due to the veterinary medicinal product's activity against the vector.

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 (including *Babesia canis canis* and *D. caninum*) cannot be completely 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:
Use with caution in dogs with pre-existing epilepsy.
In the absence of available data, the 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 for shorter intervals has not been tested.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
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.
Hypersensitivity reactions in humans have been reported.
Do not eat, drink or smoke while handling the veterinary medicinal product.

Wash hands thoroughly with soap and water immediately after use of the veterinary medicinal product.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dog:

Common (1 to 10 animals / 100 animals treated):	Gastrointestinal effects (such as Anorexia, Hypersalivation, Diarrhoea, Emesis) [#].
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Lethargy; 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

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 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 oral use.

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

Bodyweight of dog (kg)	**Strength and number of tablets 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

The chewable tablets should not be broken or divided.

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

Method of administration
Administer the veterinary medicinal product at or around the time of feeding.
The chewable tablet is well accepted by most dogs. If the tablet is not taken up voluntarily by the dog it can also be given with food or directly into the mouth. The dog should be observed during administration to confirm that the tablet is swallowed.

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 flea infestation, the veterinary medicinal product should be administered at intervals of 12 weeks. For optimal control of tick infestation, the timing of retreatment depends on the tick species. See section 3.2.
For the treatment of *Demodex canis* mite infestations, a single dose of the veterinary medicinal product should be administered. 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 administered. 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 oral administration to puppies aged 8 – 9 weeks and weighing 2.0 – 3.6 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).

The veterinary medicinal product was well tolerated in Collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the 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: QP53BE02

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.

Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* by killing the ticks within 48 hours, before disease transmission occurs.

Fluralaner reduces the risk of infection with *D. caninum* via transmission by *Ctenocephalides felis* by killing the fleas before disease transmission occurs.

The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for *I. ricinus* and 48 hours for *D. reticulatus* ticks. The onset of acaricidal efficacy against *I. hexagonus* ticks was demonstrated 7 days after treatment.

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

Following oral administration, fluralaner is readily absorbed reaching maximum plasma concentrations within 1 day. Food enhances the absorption. Fluralaner is systemically distributed and reaches the highest concentrations in fat, followed by liver, kidney and muscle. The prolonged persistence and slow elimination from plasma ($t_{1/2}$ = 12 days) and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval. Individual variation in C_{max} and $t_{1/2}$ was observed. The major route of elimination is the excretion of unchanged fluralaner in faeces (~90% of the dose). Renal clearance is the minor route of elimination.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Cardboard box with 1 aluminium foil blister sealed with PET aluminium foil lid stock containing 1, 2 or 4 chewable tablets.
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/2/13/158/001-015

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).

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 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):

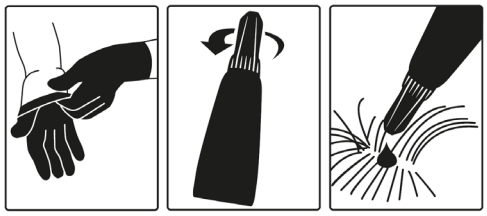
Body weight of dog (kg)	**Strength and number of pipettes to be administered**				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1 000 mg	Bravecto 1 400 mg
2 - 4.5	1				

>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.

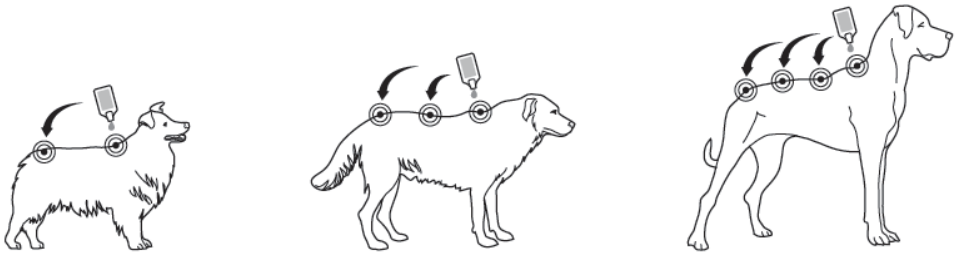
Method of administration

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).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 112.5 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto 250 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto 500 mg spot-on solution for large cats (>6.25 – 12.5 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 small cats 1.2 – 2.8 kg	0.4	112.5
for medium-sized cats >2.8 – 6.25 kg	0.89	250
for large cats >6.25 – 12.5 kg	1.79	500

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

Cat

3.2 Indications for use for each target species

For the treatment of tick and flea infestations in cats.

This veterinary medicinal product is a systemic insecticide and acaricide that provides immediate and persistent flea (*Ctenocephalides felis*) and tick (*Ixodes ricinus)* 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 infestations with ear mites (*Otodectes cynotis*).

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.
In the absence of available data, this veterinary medicinal product should not be used on kittens less than 9 weeks old and /or cats weighing less than 1.2 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.
Do not allow recently treated animals to groom each other.

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:
Not applicable.

3.6 Adverse events

Cat:

Common (1 to 10 animals / 100 animals treated):	Skin reactions at the application site (such as Erythema, Pruritus, Alopecia) [#]
Uncommon (1 to 10 animals / 1 000 animals treated):	Muscle tremor, Lethargy, Anorexia, Emesis, Hypersalivation
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	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 has not been established during pregnancy and lactation. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

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.

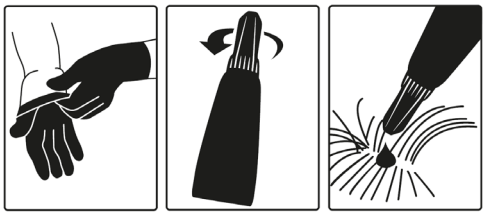
The veterinary medicinal product should be administered in accordance with the following table (corresponding to a dose of 40 – 94 mg fluralaner/kg body weight):

Body weight of cat (kg)	**Strength and number of pipettes to be administered**		
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg
1.2 – 2.8	1		
>2.8 – 6.25		1	
>6.25 – 12.5			1

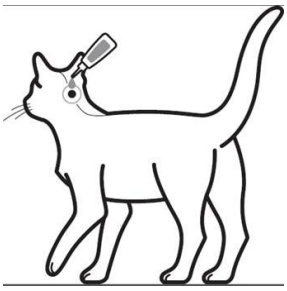
For cats above 12.5 kg body weight, use a combination of two pipettes that most closely matches the body weight.
Underdosing could result in ineffective use and may favour resistance development.

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 twist-and-use 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 cat should be standing or lying with its back horizontal for easy application. Place the pipette tip on the base of the skull of the cat.



Step 3: Squeeze the pipette gently and apply the entire contents directly to the cat's skin. The veterinary medicinal product should be applied on cats up to 6.25 kg body weight in one spot at the base of the skull and in two spots on cats greater than 6.25 kg body weight.

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 ear mite infestations *(Otodectes cynotis)*, a single dose of the veterinary medicinal product should be applied. A further veterinary examination 28 days after treatment is recommended as some animals may require further treatment with an alternative veterinary medicinal product.

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

No adverse reactions were observed following topical administration to kittens aged 9 - 13 weeks and weighing 0.9 - 1.9 kg treated with overdoses of up to 5 times the maximum recommended dose (93 mg, 279 mg and 465 mg fluralaner/kg body weight) on three occasions at shorter intervals than recommended (8-week intervals).

Oral uptake of the veterinary medicinal product at the maximum recommended dose of 93 mg fluralaner/kg body weight was well tolerated in cats, apart from some self-limiting salivation and coughing or vomiting immediately after administration.

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.), fleas (*Ctenocephalides* spp.) and ear mites (*Otodectes cynotis*) on the cat.

The onset of efficacy is within 12 hours for fleas (*C. felis*) and within 48 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 cats have access.

Newly emerged fleas on a cat 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 systemically absorbed from the topical administration site, reaching maximum concentrations in plasma between 3 and 21 days after administration. The prolonged persistence and slow elimination from plasma ($t_{1/2}$ = 12 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 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/2/13/158/018-019	112.5 mg
EU/2/13/158/022-023	250 mg
EU/2/13/158/026-027	500 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).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 150 mg/ml powder and solvent for suspension for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Powder vial:

Active substance:
Fluralaner 2.51 g

White to pale yellow powder.

Solvent vial:

Each ml of solvent contains:

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol	22.3 mg
Carmellose sodium	
Poloxamer 124	
Disodium phosphate dihydrate	
Hydrochloric acid, concentrated	
Sodium hydroxide	
Water for injections	

Clear to opaque viscous solution.

Reconstituted suspension:

Each ml of reconstituted suspension contains:

Active substance:
Fluralaner 150 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol	20 mg
Carmellose sodium	
Poloxamer 124	
Disodium phosphate dihydrate	

Hydrochloric acid, concentrated	
Sodium hydroxide	
Water for injections	

3. CLINICAL INFORMATION

3.1 Target species

Dogs

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 months,
- persistent tick killing activity from 3 days to 12 months after treatment for *Ixodes ricinus, Ixodes hexagonus,* and *Dermacentor reticulatus,*
- persistent tick killing activity from 4 days to 12 months after treatment for *Rhipicephalus sanguineus.*

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 reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* from day 3 after treatment for up to 12 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for up to 12 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

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 (including *Babesia canis canis* and *D. caninum*) cannot be completely excluded.

Unnecessary use of antiparasitics, or use deviating from the instructions given, 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 (having regard to the duration of the effect of the product of 12 months), 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:
Safety of the product has not been assessed in dogs with pre-existing epilepsy. Therefore, use with caution in such dogs based on a benefit/risk assessment by the responsible veterinarian.
In the absence of available data, the veterinary medicinal product should not be used on dogs less than 6 months old.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Hypersensitivity reactions to fluralaner or benzyl alcohol in humans have been reported, which can potentially be serious. Also, injection site reactions may occur. Care should be taken to avoid accidental self-injection and dermal exposure when administering this veterinary medicinal product. In case of accidental self-injection with adverse effects, hypersensitivity reactions or injection site reactions, contact a physician and show the label or package leaflet. Wash hands after use.
This veterinary medicinal product is to be administered only by veterinarians or under their close supervision.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Common (1 to 10 animals / 100 animals treated)	Injection site swelling[1]
Uncommon (1 to 10 animals / 1,000 animals treated)	Decreased appetite Tiredness Hyperaemic mucous membranes
Very rare (<1 animal / 10 000 animals treated, including isolated reports)	Muscle tremor, Ataxia, Convulsion

[1]Palpable and/or visual swellings, non-inflammatory, non-painful, self-resolving over time

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 Interaction with other medicinal products and other forms of interaction

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 clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products were observed.

3.9 Administration routes and dosage

Subcutaneous use.

Administer 0.1 ml of reconstituted suspension per kg body weight (equivalent to 15 mg fluralaner per kg body weight) subcutaneously, e.g. between the shoulder blades (dorso-scapular region) of the dog. The dog should be weighed at the time of dosing to calculate an accurate dose.
Underdosing could result in ineffective use and may favour development of resistance.

The following table may be used as a dosage guide:

Body weight (kg)	Volume of the reconstituted suspension (ml)
5	0.5
10	1
15	1.5
20	2
25	2.5
30	3
35	3.5
40	4
45	4.5
50	5
55	5.5
60	6

Calculate the dose accordingly for dogs weighing less than 5 kg or more than 60 kg.

Reconstitution of the suspension before first use:
Reconstitute 1 vial of powder with 15 ml of solvent. It is recommended to use an 18 G sterile transfer needle and a sterile 20 ml syringe for the reconstitution of the product.

1. Shake the fluralaner powder vial to break up any aggregates prior to reconstitution.
2. Invert the solvent vial at least 3 times until the content is visibly uniform.
3. First inject up to 14 ml of air into the solvent vial, then withdraw **15 ml** of the solvent from the vial (image A). **There is more solvent supplied in the vial than required for reconstitution.** Discard the vial with the rest of the solvent.
4. Insert the 25 G vent needle into the top of the fluralaner powder vial (image B).
5. **While rotating the vial horizontally in your hand,** slowly transfer the 15 ml of solvent into the fluralaner powder vial to ensure complete wetting of the powder (image C).

A **B** **C**

6. Once the solvent has been added, remove the vent needle and the transfer needle from the fluralaner powder vial. Discard the needles.

7. Shake the vial vigorously for at least 30 seconds until a thoroughly mixed suspension is formed. The reconstituted product is an opaque white to pale yellow slightly viscous suspension, practically free of aggregates.
8. The expiry date printed on the label of the glass vial refers to the powder as packaged for sale. After reconstitution, the suspension must be discarded within 3 months from the date of reconstitution. Write the discard date on the label of the glass vial.

Method of administration of the reconstituted suspension to the dog:

1. Determine the dose to be administered based on the dog's body weight.
2. Use a sterile syringe and a sterile 18 G needle for administration.
3. The fluralaner powder will separate out of suspension upon standing. Before every use, shake the reconstituted vial vigorously for 30 seconds to achieve a uniform suspension.
4. It may be necessary to inject air into the vial prior to dosing.
5. To maintain a uniform suspension and accurate dosing, the dose should be administered within approximately 5 minutes after drawing it into the dosing syringe.
6. Inject the product subcutaneously, e.g. in the dorso-scapular region.

Do not puncture the stopper of the vial containing the reconstituted suspension more than 20 times. For reconstitution after settling, shake the vial vigorously for at least 30 seconds to achieve a uniform suspension.

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. Treatment with this veterinary medicinal product may begin at any time of the year and can continue without interruption. See section 3.4.

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

Following the subcutaneous administration of 3 and 5 times the recommended dose of 15 mg fluralaner/kg body weight every 4 months for a total of 6 doses (Days 1, 120, 239, 358, 477 and 596) to 6 months old puppies, the only treatment-related finding was limited to injection site swellings that resolved over time.

The active substance 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). Since the peak systemic exposure to fluralaner after subcutaneous administration is not higher compared to oral administration, the subcutaneous injection of the veterinary medicinal product is considered safe in MDR1(-/-) dogs.

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: QP53BE02

4.2 Pharmacodynamics

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp*., Dermacentor* spp. and *Rhipicephalus sanguineus*) and fleas (*Ctenocephalides* spp.) on dogs.

Fluralaner reduces the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* by killing the ticks within 48 hours, before disease transmission occurs.

Fluralaner reduces the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* by killing the fleas before disease transmission occurs.

I. ricinus and *D. reticulatus* ticks already present on the dog prior to administration of the veterinary medicinal product are killed within 72 hours. *R. sanguineus* ticks already present on the dog prior to administration of the veterinary medicinal product are killed within 96 hours. Ticks newly infested are killed within 48 hours from one week through 12 months after treatment.

Fleas already present on the dog prior to administration of the veterinary medicinal product are killed within 48 hours. Fleas newly infested are killed within 24 hours from one week through 12 months after treatment.

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 systemically absorbed from the injection site, with median T_{max} observed on day 37 (range day 30 – day 72). The half-life in blood ranges from 92 to 170 days in 6 months old puppies. The prolonged persistence and slow elimination from plasma and the lack of extensive metabolism provide effective concentrations of fluralaner for the duration of the inter-dosing interval. Unchanged fluralaner is excreted in faeces and to a very low extent in urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after reconstitution according to directions: 3 months

5.3 Special precautions for storage

This veterinary medicinal product as packaged for sale does not require any special temperature storage conditions.
After reconstitution, store below 30 °C.

5.4 Nature and composition of immediate packaging

Type I glass vials closed with bromobutyl rubber stoppers and sealed with aluminium flip-off caps.

Each cardboard box contains 1, 2, 5 or 10 sets of a fluralaner powder vial (2.51 g fluralaner), a solvent vial (16 ml solvent), and a sterile 25 G vent needle.
Not all pack-sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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/2/13/158/032-035

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD month YYYY}

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

{DD month 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).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner
1 000 mg fluralaner
1 400 mg fluralaner

3. PACKAGE SIZE

1 chewable tablet
2 chewable tablets
4 chewable tablets

4. TARGET SPECIES

Dog

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/13/158/001 (112.5 mg, 1 tablet)
EU/2/13/158/002 (112.5 mg, 2 tablets)
EU/2/13/158/003 (112.5 mg, 4 tablets)
EU/2/13/158/004 (250 mg, 1 tablet)
EU/2/13/158/005 (250 mg, 2 tablets)
EU/2/13/158/006 (250 mg, 4 tablets)
EU/2/13/158/007 (500 mg, 1 tablet)
EU/2/13/158/008 (500 mg, 2 tablets)
EU/2/13/158/009 (500 mg, 4 tablets)
EU/2/13/158/010 (1 000 mg, 1 tablet)
EU/2/13/158/011 (1 000 mg, 2 tablets)
EU/2/13/158/012 (1 000 mg, 4 tablets)
EU/2/13/158/013 (1 400 mg, 1 tablet)
EU/2/13/158/014 (1 400 mg, 2 tablets)
EU/2/13/158/015 (1 400 mg, 4 tablets)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

112.5 mg (2 – 4.5 kg)
250 mg (>4.5 – 10 kg)
500 mg (>10 – 20 kg)
1 000 mg (>20 – 40 kg)
1 400 mg (>40 – 56 kg)
fluralaner

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box

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. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner
1 000 mg fluralaner
1 400 mg fluralaner

3. PACKAGE SIZE

1 x 0.4 ml
1 x 0.89 ml
1 x 1.79 ml
1 x 3.57 ml
1 x 5.0 ml
2 x 0.4 ml
2 x 0.89 ml
2 x 1.79 ml
2 x 3.57 ml
2 x 5.0 ml

4. TARGET SPECIES

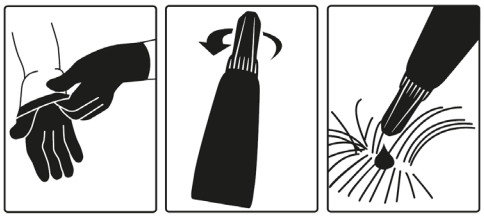
Dog

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Spot-on use.
Keep the veterinary medicinal product in the original packaging until use in order to prevent children from getting access to the veterinary medicinal product. Avoid contact with skin, mouth and/or eye. Do not contact the application site until it is no longer noticeable.
Wear gloves when handling and administering this veterinary medicinal product. Read package leaflet for full user safety information.

Cap does not come off.



7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/13/158/016 (112.5 mg, 1 pipette)
EU/2/13/158/017 (112.5 mg, 2 pipettes)
EU/2/13/158/020 (250 mg, 1 pipette)
EU/2/13/158/021 (250 mg, 2 pipettes)
EU/2/13/158/024 (500 mg, 1 pipette)
EU/2/13/158/025 (500 mg, 2 pipettes)
EU/2/13/158/028 (1 000 mg, 1 pipette)
EU/2/13/158/029 (1 000 mg, 2 pipettes)
EU/2/13/158/030 (1 400 mg, 1 pipette)
EU/2/13/158/031 (1 400 mg, 2 pipettes)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Sachet

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. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner
1 000 mg fluralaner
1 400 mg fluralaner

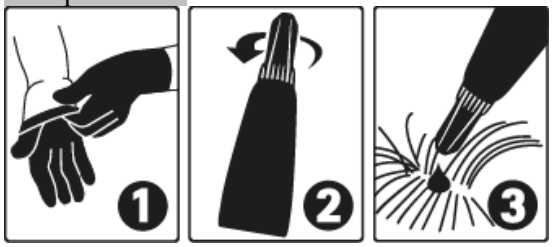
0.4 ml
0.89 ml
1.79 ml
3.57 ml
5.0 ml

3. TARGET SPECIES

Dog

4. ROUTES OF ADMINISTRATION

For spot-on use



1. Put on gloves. 2. Rotate cap (cap cannot be removed). 3. Apply to skin.
Keep the pipette in the sachet until use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner
1 000 mg fluralaner
1 400 mg fluralaner

0.4 ml
0.89 ml
1.79 ml
3.57 ml
5.0 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 112.5 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto 250 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto 500 mg spot-on solution for large cats (>6.25 – 12.5 kg)

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner

3. PACKAGE SIZE

1 x 0.4 ml
1 x 0.89 ml
1 x 1.79 ml
2 x 0.4 ml
2 x 0.89 ml
2 x 1.79 ml

4. TARGET SPECIES

Cat

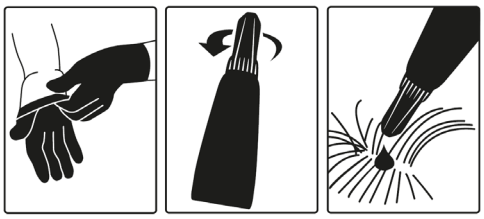
5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Spot-on use.

Keep the veterinary medicinal product in the original packaging until use in order to prevent children from getting access to the veterinary medicinal product. Avoid contact with skin, mouth and/or eye. Do not contact the application site until it is no longer noticeable.
Wear gloves when handling and administering this veterinary medicinal product. Read package leaflet for full user safety information.

Cap does not come off.



7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/13/158/018 (112.5 mg, 1 pipette)
EU/2/13/158/019 (112.5 mg, 2 pipettes)
EU/2/13/158/022 (250 mg, 1 pipette)
EU/2/13/158/023 (250 mg, 2 pipettes)
EU/2/13/158/026 (500 mg, 1 pipette)
EU/2/13/158/027 (500 mg, 2 pipettes)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Sachet

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 112.5 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto 250 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto 500 mg spot-on solution for large cats (>6.25 – 12.5 kg)

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner

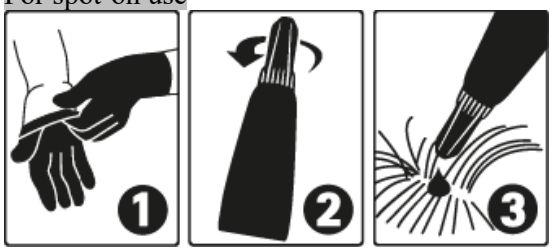
0.4 ml
0.89 ml
1.79 ml

3. TARGET SPECIES

Cat

4. ROUTES OF ADMINISTRATION

For spot-on use



1. Put on gloves. 2. Rotate cap (cap cannot be removed). 3. Apply to skin.
Keep the pipette in the sachet until use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp. {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner

0.4 ml
0.89 ml
1.79 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto 150 mg/ml powder and solvent for suspension for injection for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

150 mg/ml fluralaner

3. PACKAGE SIZE

1 vial containing powder, 1 vial containing solvent, 1 vent needle
2 vials containing powder, 2 vials containing solvent, 2 vent needles
5 vials containing powder, 5 vials containing solvent, 5 vent needles
10 vials containing powder, 10 vials containing solvent, 10 vent needles

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

{The following diagrams are printed on the inside of the cardboard box - visible only after opening}

The enclosed vent needle is not intended for product administration.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once reconstituted use the suspension within 3 months.

9. SPECIAL STORAGE PRECAUTIONS

After reconstitution, store below 30 °C.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/13/158/032 (1 x: powder, solvent, vent needle)
EU/2/13/158/033 (2 x: powder, solvent, vent needle)
EU/2/13/158/034 (5 x: powder, solvent, vent needle)
EU/2/13/158/035 (10 x: powder, solvent, vent needle)

15. BATCH NUMBER

Lot {number}

QR code to be included mix.bravecto.com

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL OF THE POWDER VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

2.51 g fluralaner
reconstituted: 150 mg/ml suspension for injection

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
After reconstitution, use within 3 months.
Discard by:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL OF THE SOLVENT VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto solvent

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

16 ml
Only use 15 ml to reconstitute the suspension. Discard the rest.

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

Each chewable tablet contains:

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

Light to dark brown tablet with a smooth or slightly rough surface and circular shape. Some marbling, speckles or both may be visible.

3. Target species

Dog

4. Indications for use

For the treatment of tick and flea infestations on dogs.

This veterinary medicinal product is a systemic insecticide and acaricide that provides
- immediate and persistent flea (*Ctenocephalides felis*) killing activity for 12 weeks,
- immediate and persistent tick killing activity for 12 weeks for *Ixodes ricinus, Dermacentor reticulatus* and *D. variabilis,*
- immediate and persistent tick killing activity for 8 weeks for *Rhipicephalus sanguineus,*
- persistent tick killing activity from 7 days to 12 weeks after treatment for *Ixodes hexagonus.*

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.

For reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* for up to 12 weeks. The effect is indirect due to the veterinary medicinal product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for up to 12 weeks. The effect is indirect due to the veterinary medicinal product's activity against the vector.

5. Contraindications

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

6. Special warnings

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 (including *Babesia canis canis* and *D. caninum*) cannot be completely 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.

Special precautions for safe use in the target species:
Use with caution in dogs with pre-existing epilepsy.
In the absence of available data, the 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 for shorter intervals has not been tested.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
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.
Hypersensitivity reactions in humans have been reported.
Do not eat, drink or smoke while handling the veterinary medicinal product.
Wash hands thoroughly with soap and water immediately after use of the veterinary medicinal product.

Pregnancy, lactation and fertility:
The veterinary medicinal product can be used in breeding, pregnant and lactating dogs.

Interaction with other medicinal products and other forms of interaction:
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 clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products were observed.

Overdose:
Safety was demonstrated in breeding, pregnant and lactating animals treated with overdoses of up to 3 times the maximum recommended dose.

Safety was demonstrated in puppies aged 8 – 9 weeks and weighing 2.0 – 3.6 kg treated with overdoses of up to 5 times the maximum recommended dose on three occasions at shorter intervals than recommended (8-week intervals).
The veterinary medicinal product was well tolerated in collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the recommended dose.

Major incompatibilities:

Not applicable.

7. Adverse events

Dog:

Common (1 to 10 animals / 100 animals treated):	Gastrointestinal effects (such as Inappetence, Drooling, Diarrhoea, Vomiting) [#].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Apathy, Muscle tremor, Ataxia, Convulsion.

[#] mild and transient

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

For oral 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 within one weight band):

Body weight of dog (kg)	**Strength and number of tablets 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 tablets that most closely matches the body weight.

Underdosing could result in ineffective use and may favour resistance development.

9. Advice on correct administration

The chewable tablets should not be broken or divided.
Administer the veterinary medicinal products at or around the time of feeding.

The chewable tablet is well accepted by most dogs. If the tablet is not taken up voluntarily by the dog it can also be given with food or directly into the mouth. The dog should be observed during administration to confirm that the tablet is swallowed.

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 flea infestation, the veterinary medicinal product should be administered at intervals of 12 weeks. For optimal control of tick infestation, the timing of retreatment depends on the tick species. See section ´Indications for use`.
For the treatment of *Demodex canis* mite infestations, a single dose of the veterinary medicinal product should be administered. 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 administered. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

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

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/13/158/001–015
Cardboard box containing 1, 2 or 4 chewable tablets.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
Тел: + 359 28193749

Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Deutschland
Tel: + 49 (0)8945614100

Eesti
Tel: + 37052196111

Ελλάδα
Τηλ: + 30 210 989 7452

España
Tel: + 34 923 19 03 45

France
Tél: + 33 (0)241228383

Hrvatska
Tel: + 385 1 6611339

Ireland
Tel: + 353 (0) 1 2970220

Ísland
Sími: + 354 535 7000

Italia
Tel: + 39 02 516861

Lietuva
Tel: + 37052196111

Luxembourg/Luxemburg
Tél/Tel: + 32 (0)2 370 94 01

Magyarország
Tel.: + 36 1 439 4597

Malta
Tel: + 39 02 516861

Nederland
Tel: + 32 (0)2 370 94 01

Norge
Tlf: + 47 55 54 37 35

Österreich
Tel: + 43 (1) 256 87 87

Polska
Tel.: + 48 22 18 32 200

Portugal
Tel: + 351 214 465 700

România
Tel: + 40 21 311 83 11

Slovenija
Tel: + 385 1 6611339

Slovenská republika
Tel: +420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Κύπρος
Τηλ: +30 210 989 7452

Latvija
Tel: + 37052196111

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

Manufacturer responsible for batch release:
Intervet Ges.m.b.H.
Siemensstrasse 107
1210 Vienna
Austria

17. Other information

The product contributes towards the control of environmental flea populations in areas to which treated dogs have access.
The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for *I. ricinus* and 48 hours for *D. reticulatus* ticks. The onset of acaricidal efficacy against *I. hexagonus* ticks was demonstrated 7 days after treatment.

PACKAGE LEAFLET

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. Composition

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

Clear colourless to yellow solution.

3. Target species

Dog

4. Indications for use

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 *C. canis*) killing activity for 12 weeks,
- 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.

5. Contraindications

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

6. Special warnings

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.

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 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 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

Pregnancy and lactation and fertility:
Can be used in breeding, pregnant and lactating dogs.

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.

Overdose:
Safety was demonstrated in puppies aged 8 – 9 weeks and weighing 2.0 – 3.7 kg treated with overdoses of up to 5 times the maximum recommended dose on three occasions at shorter intervals than recommended (8-week intervals).
Safety was demonstrated in breeding, pregnant and lactating animals treated with overdoses of up to 3 times the maximum recommended dose.
This veterinary medicinal product was well tolerated in collies with a deficient multidrug-resistance-protein 1 (MDR1 -/-) following single oral administration at 3 times the maximum recommended dose.

Major incompatibilities:
None known.

7. 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):	Apathy, Inappetence Vomiting Muscle tremor, Ataxia (Incoordination), Convulsion

[#] mild and transient

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

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):

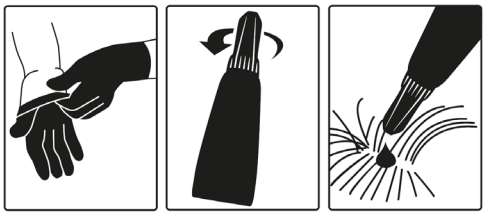
Body weight of dog (kg)	Strength and number of pipettes to be administered				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1 000 mg	Bravecto 1 400 mg
2 - 4.5	1				
>4.5 - 10		1			
>10 - 20			1		
>20 - 40				1	
>40 - 56					1

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.

9. Advice on correct administration

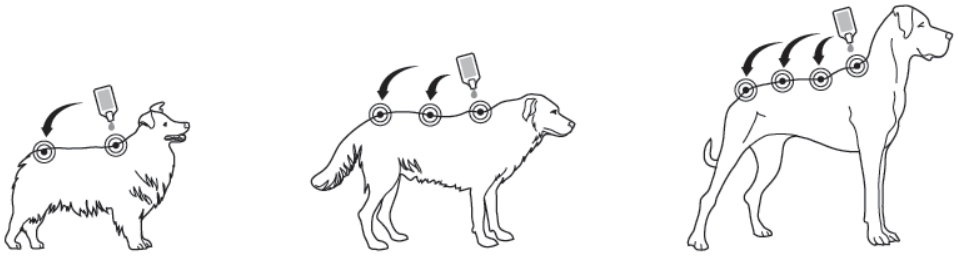
Method of administration

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 twist-and-use 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.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
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.

Do not use this veterinary medicinal product after the expiry date stated on the packaging after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

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
Each cardboard box contains 1 or 2 pipettes and a pair of gloves per pipette.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

België/Belgique/Belgien
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Република България
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Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Deutschland
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Eesti
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Ελλάδα
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España
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France
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Hrvatska
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Ireland
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Lietuva
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Luxembourg/Luxemburg
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Magyarország
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Malta
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Nederland
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Norge
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Österreich
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Polska
Tel.: + 48 22 18 32 200

Portugal
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România
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Slovenija
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Slovenská republika
Tel: +420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

Manufacturer responsible for batch release:
Intervet Productions S.A.
Rue de Lyons

27460 Igoville
France

17. Other information

The veterinary medicinal product contributes towards the control of environmental flea populations in areas to which treated dogs have access.
The onset of efficacy is within 8 hours for fleas (*C. felis*) and 12 hours for ticks (*I. ricinus*).

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Bravecto 112.5 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto 250 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto 500 mg spot-on solution for large cats (>6.25 – 12.5 kg)

2. Composition

Each ml contains 280 mg fluralaner.
Each pipette delivers:

Bravecto spot-on solution	**Pipette content (ml)**	**Fluralaner (mg)**
for small cats 1.2 – 2.8 kg	0.4	112.5
for medium-sized cats >2.8 – 6.25 kg	0.89	250
for large cats >6.25 – 12.5 kg	1.79	500

Clear colourless to yellow solution.

3. Target species

Cat

4. Indications for use

For the treatment of tick and flea infestations in cats.

This veterinary medicinal product is a systemic insecticide and acaricide that provides immediate and persistent flea (*Ctenocephalides felis*) and tick (*Ixodes ricinus)* 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 infestations with ear mites (*Otodectes cynotis*).

5. Contraindications

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

6. Special warnings

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.

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.
In the absence of available data, this veterinary medicinal product should not be used on kittens less than 9 weeks old and /or cats weighing less than 1.2 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.
Do not allow recently treated animals to groom each other.

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.

Pregnancy and lactation and fertility:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

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.

Overdose:
Safety was demonstrated in kittens aged 9 - 13 weeks and weighing 0.9 - 1.9 kg treated with overdoses of up to 5 times the maximum recommended dose on three occasions at shorter intervals than recommended (8-week intervals).
Oral uptake of the veterinary medicinal product at the maximum recommended dose was well tolerated in cats, apart from some self-limiting salivation and coughing or vomiting immediately after administration.

Major incompatibilities:
None known.

7. Adverse events

Cat:

Common (1 to 10 animals / 100 animals treated):	Skin reactions at the application site (such as Erythema, Itching, Alopecia) [#]
Uncommon (1 to 10 animals / 1,000 animals treated):	Muscle tremor, Apathy, Inappetence, Vomiting, Drooling
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Convulsion

[#] mild and transient

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

For spot-on use.

The veterinary medicinal product should be administered in accordance with the following table (corresponding to a dose of 40 – 94 mg fluralaner/kg body weight):

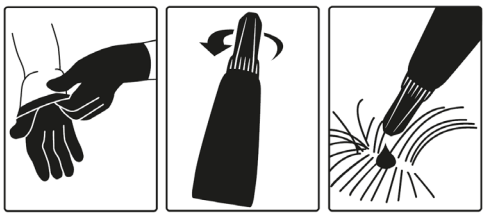
Body weight of cat (kg)	**Strength and number of pipettes to be administered**		
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg
1.2 – 2.8	1		
>2.8 – 6.25		1	
>6.25 – 12.5			1

For cats above 12.5 kg body weight, use a combination of two pipettes that most closely matches the body weight.

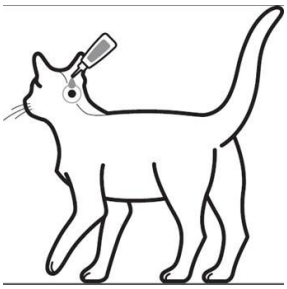
Underdosing could result in ineffective use and may favour resistance development.

9. Advice on correct administration

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 twist-and-use 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 cat should be standing or lying with its back horizontal for easy application. Place the pipette tip on the base of the skull of the cat.

Step 3: Squeeze the pipette gently and apply the entire contents directly to the cat's skin. The veterinary medicinal product should be applied on cats up to 6.25 kg body weight in one spot at the base of the skull and in two spots on cats greater than 6.25 kg body weight.

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 ear mite infestations *(Otodectes cynotis)*, a single dose of the veterinary medicinal product should be applied. A further veterinary examination 28 days after treatment is recommended as some animals may require further treatment with an alternative veterinary medicinal product.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

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.

Do not use this veterinary medicinal product after the expiry date stated on the packaging after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/13/158/018-019 112.5 mg
EU/2/13/158/022-023 250 mg
EU/2/13/158/026-027 500 mg
Each cardboard box contains 1 or 2 pipettes and a pair of gloves per pipette.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
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Danmark
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Deutschland
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Eesti
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Lietuva
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Luxembourg/Luxemburg
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Nederland
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España
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France
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Hrvatska
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Ireland
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Slovenská republika
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Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
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United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

Manufacturer responsible for batch release:
Intervet Productions S.A.
Rue de Lyons
27460 Igoville
France

17. Other information

The veterinary medicinal product contributes towards the control of environmental flea populations in areas to which treated cats have access.
The onset of efficacy is within 12 hours for fleas (*C. felis*) and within 48 hours for ticks (*I. ricinus*).

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Bravecto 150 mg/ml powder and solvent for suspension for injection for dogs

2. Composition

Powder vial:	**Solvent vial:**	**Reconstituted suspension:**
Each vial contains: Active substance: Fluralaner 2.51 g	Each ml contains: Excipients: Benzyl alcohol 22.3 mg	Each ml contains: Active substance: Fluralaner 150 mg Excipients: Benzyl alcohol 20 mg
White to pale yellow powder.	Clear to opaque viscous solution.	Opaque white to pale yellow, slightly viscous suspension.

3. Target species

Dogs

4. Indications for use

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 months
- persistent tick killing activity from 3 days to 12 months after treatment for *Ixodes ricinus, Ixodes hexagonus,* and *Dermacentor reticulatus*
- persistent tick killing activity from 4 days to 12 months after treatment for *Rhipicephalus sanguineus.*

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 reduction of the risk of infection with *Babesia canis canis* via transmission by *Dermacentor reticulatus* from day 3 after treatment for up to 12 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

For reduction of the risk of infection with *Dipylidium caninum* via transmission by *Ctenocephalides felis* for up to 12 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

5. Contraindications

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

6. Special warnings

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 (including *Babesia canis canis* and *D. caninum*) cannot be completely excluded.
Unnecessary use of antiparasitics, or use deviating from the instructions given, 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 (having regard to the duration of the effect of the product of 12 months), 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.

Special precautions for safe use in the target species:
Safety of the product has not been assessed in dogs with pre-existing epilepsy. Therefore, use with caution in such dogs based on a benefit/risk assessment by the responsible veterinarian.
In the absence of available data, the veterinary medicinal product should not be used on dogs less than 6 months old.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Hypersensitivity reactions to fluralaner or benzyl alcohol in humans have been reported, which can potentially be serious. Also, injection site reactions may occur. Care should be taken to avoid accidental self-injection and dermal exposure when administering this veterinary medicinal product. In case of accidental self-injection with adverse effects, hypersensitivity reactions or injection site reactions, contact a physician and show the label or package leaflet. Wash hands after use.
This veterinary medicinal product is to be administered only by veterinarians or under their close supervision.

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

Interaction with other medicinal products and other forms of interaction:
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 clinical field testing, no interactions between the veterinary medicinal product and routinely used veterinary medicinal products including vaccinations were observed.

Overdose:
Following the subcutaneous administration of 3 and 5 times the recommended dose of 15 mg fluralaner/kg body weight every 4 months for a total of 6 doses (Days 1, 120, 239, 358, 477 and 596) to 6 months old puppies, the only treatment-related finding was limited to injection site swellings that resolved over time.
The active substance 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). Since the peak systemic exposure to fluralaner after subcutaneous administration is not higher compared to oral administration, the subcutaneous injection of the veterinary medicinal product is considered safe in MDR1(-/-) dogs.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Dogs:

1. Common (1 to 10 animals / 100 animals treated):
2. Injection site swelling[1]
3. Uncommon (1 to 10 animals / 1,000 animals treated):
4. Decreased appetite, Tiredness, Hyperaemic mucous membranes
Very rare (<1 animal / 10 000 animals treated, including isolated reports):
5. Muscle tremor, Ataxia (Incoordination), Convulsion

6. [1]Palpable and/or visual swellings, non-inflammatory, non-painful, self-resolving over time
7.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

Subcutaneous use.
Administer 0.1 ml of the reconstituted suspension per kg body weight (equivalent to 15 mg fluralaner per kg body weight) subcutaneously, e.g. between the shoulder blades (dorso-scapular region) of the dog. The dog should be weighed at the time of dosing to calculate an accurate dose.
Underdosing could result in ineffective use and may favour resistance development.

The following table may be used as a dosage guide:

Body weight of the dog (kg)	Dose volume of the reconstituted suspension (ml)
5	0.5
10	1
15	1.5
20	2
25	2.5
30	3
35	3.5
40	4
45	4.5
50	5
55	5.5
60	6

Calculate the dose accordingly for dogs weighing less than 5 kg or more than 60 kg.

9. Advice on correct administration

8.

9. Reconstitution of the suspension before first use:

Reconstitute 1 vial of powder with 15 ml of solvent. It is recommended to use an 18 G sterile transfer needle and a sterile 20 ml syringe for the reconstitution of the product.

10.

1. Shake the fluralaner powder vial to break up any aggregates prior to reconstitution.
2. Invert the solvent vial at least 3 times until the content is visibly uniform.
3. First inject up to 14 ml of air into the solvent vial, then withdraw **15 ml** of the solvent from the vial (image A). **There is more solvent supplied in the vial than required for reconstitution.**

Discard the vial with the rest of the solvent.

4. Insert the 25 G vent needle into the top of the fluralaner powder vial (image B).
5. **While rotating the vial horizontally in your hand,** slowly transfer the 15 ml of solvent into the fluralaner powder vial to ensure complete wetting of the powder (image C).

A **B** **C**

6. Once the solvent has been added, remove the vent needle and the transfer needle from the fluralaner powder vial. Discard the needles.
7. Shake the vial vigorously for at least 30 seconds until a thoroughly mixed suspension is formed. The reconstituted product is an opaque white to pale yellow slightly viscous suspension, practically free of aggregates.
8. The expiry date printed on the label of the glass vial refers to the powder as packaged for sale. After reconstitution, the suspension must be discarded within 3 months from the date of reconstitution. Write the discard date on the label of the glass vial.

Method of administration of the reconstituted suspension to the dog:

1. Determine the dose to be administered based on the dog's body weight.
2. Use a sterile syringe and a sterile 18 G needle for administration.
3. The fluralaner powder will separate out of suspension upon standing. Before every use, shake the reconstituted vial vigorously for 30 seconds to achieve a uniform suspension.
4. It may be necessary to inject air into the vial prior to dosing.
5. To maintain a uniform suspension and accurate dosing, the dose should be administered within approximately 5 minutes after drawing it into the dosing syringe.
6. Inject the product subcutaneously, e.g. in the dorso-scapular region.

Do not puncture the stopper of the vial containing the reconstituted suspension more than 20 times.
For reconstitution after settling, shake the vial vigorously for at least 30 seconds to achieve a uniform suspension.

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. Treatment with this veterinary medicinal product may begin at any time of the year and can continue without interruption. See also section "Special warnings".

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
This veterinary medicinal product as packaged for sale does not require any special temperature storage conditions.
After reconstitution, store below 30 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.
Shelf life after reconstitution of the suspension according to directions: 3 months.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
This 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 applicable national collection systems. These measures should help to protect the environment.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/13/158/032-035
Each cardboard box contains 1, 2, 5 or 10 powder vial(s), solvent vial(s), and sterile vent needle(s).
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

DD month YYYY

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Intervet International B.V., Wim de Körverstraat 35, 5831 AN Boxmeer, The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
Тел: + 359 28193749

Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Lietuva
Tel: + 37052196111

Luxembourg/Luxemburg
Tél/Tel: + 32 (0)2 370 94 01

Magyarország
Tel.: + 36 1 439 4597

Malta
Tel: + 39 02 516861

Deutschland
Tel: + 49 (0)8945614100

Eesti
Tel: + 37052196111

Ελλάδα
Τηλ: + 30 210 989 7452

España
Tel: + 34 923 19 03 45

France
Tél: + 33 (0)241228383

Hrvatska
Tel: + 385 1 6611339

Ireland
Tel: + 353 (0) 1 2970220

Ísland
Sími: + 354 535 7000

Italia
Tel: + 39 02 516861

Κύπρος
Τηλ: + 30 210 989 7452

Latvija
Tel: + 37052196111

Nederland
Tel: + 32 (0)2 370 94 01

Norge
Tlf: + 47 55 54 37 35

Österreich
Tel: + 43 (1) 256 87 87

Polska
Tel.: + 48 22 18 32 200

Portugal
Tel: + 351 214 465 700

România
Tel: + 40 21 311 83 11

Slovenija
Tel: + 385 1 6611339

Slovenská republika
Tel: + 420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

Manufacturer responsible for batch release:
Vet Pharma Friesoythe GmbH, Sedelsberger Strasse 2-4, 26169 Friesoythe, Germany

17. Other information

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

18. *I. ricinus* and *D. reticulatus* ticks already present on the dog prior to administration of the veterinary medicinal product are killed within 72 hours. *R. sanguineus* ticks already present on the dog prior to administration of the veterinary medicinal product are killed within 96 hours. Ticks newly infested are killed within 48 hours from one week through 12 months after treatment.
19.
Fleas already present on the dog prior to administration of the veterinary medicinal product are killed within 48 hours. Fleas newly infested are killed within 24 hours from one week through 12 months after treatment.
20.
QR code to be included mix.bravecto.com