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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the 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*.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for ticks (*I. ricinus*).

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

4.3 Contraindications

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

4.4 Special warnings for each target species

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.

4.5 Special precautions for use

Special precautions for use in animals

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 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 product in the original packaging until use, in order to prevent children from getting direct access to the product.
Do not eat, drink or smoke while handling the product.
Wash hands thoroughly with soap and water immediately after use of the product.

4.6 Adverse reactions (frequency and seriousness)

Mild and transient gastrointestinal effects such as diarrhoea, vomiting, inappetence, and drooling were commonly observed in clinical trials (1.6% of treated dogs).

Convulsions and lethargy has been reported very rarely in spontaneous reports.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

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.

4.8 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 Bravecto chewable tablets for dogs and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

For oral use.

Bravecto 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 bodyweight, use a combination of two tablets that most closely matches the bodyweight.

Method of administration
Administer Bravecto chewable tablets at or around the time of feeding.
Bravecto is a chewable tablet and 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 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 4.2.

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

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 bodyweight) 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 bodyweight 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 bodyweight). No treatment-related clinical signs were observed.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.

ATCvet code: QP53BE02.

5.1 Pharmacodynamic properties

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

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 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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pork liver flavour
Sucrose
Maize starch
Sodium lauryl sulfate
Disodium embonate monohydrate
Magnesium stearate
Aspartame
Glycerol
Soya-bean oil
Macrogol 3350

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4. Special precautions for storage

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

6.5 Nature and composition of immediate packaging

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.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/158/001-015

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11/02/2014
Date of last renewal:

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

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:

	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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on-solution.
Clear colourless to yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the 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 product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

4.3 Contraindications

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

4.4 Special warnings for each target species

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.

4.5 Special precautions for use

Special precautions for use in animals
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 product should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
This 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
This product is harmful after ingestion. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the 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 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. Contact may occur either directly, when handling the product, or when handling the treated animal. In order to avoid contact, disposable protective gloves obtained with this product at the point of sale must be worn when handling and administering the product.
If skin contact does occur, wash the affected area immediately with soap and water. In some cases, soap and water is not sufficient to remove the product spilled on the fingers, therefore gloves must be used.
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 product packaging.
This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.
The 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 product using paper tissue and clean the area with detergent.
Hypersensitivity reactions to the product have been reported in a small number of people. The product should not be used by persons with a hypersensitivity to the active substance or to any of the excipients (see contraindications, section 4.3). 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.

4.6 Adverse reactions (frequency and seriousness)

Mild and transient skin reactions such as erythema or alopecia at the application site were commonly observed in clinical trials (1.2% of treated dogs).

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

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.

4.8 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 Bravecto spot-on solution for dogs and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

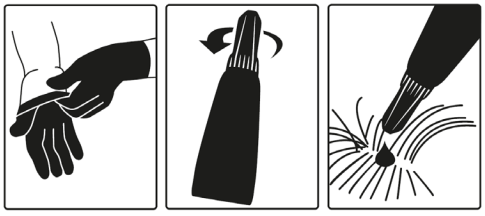
For spot-on use.

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

Bodyweight 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.

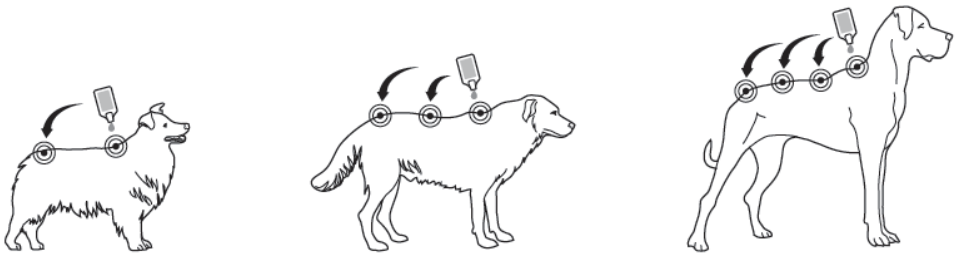
Method of administration



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 optimal control of tick and flea infestation, the product should be administered at intervals of 12 weeks.

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

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 bodyweight) 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 bodyweight 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 bodyweight). No treatment-related clinical signs were observed.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use.
ATCvet code: QP53B E02.

5.1 Pharmacodynamic properties

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

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dimethylacetamide
Glycofurol
Diethyltoluamide (DEET)
Acetone

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4. 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.

6.5 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.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. 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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11/02/2014

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

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:

	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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spot-on-solution.
Clear colourless to yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cats.

4.2 Indications for use, specifying the 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 product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

4.3 Contraindications

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

4.4 Special warnings for each target species

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.

4.5 Special precautions for use

Special precautions for use in animals
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 kitten less than 11 weeks old and /or cats weighing less than 1.2 kg.
The product should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
This 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
This product is harmful after ingestion. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the 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 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. Contact may occur either directly, when handling the product, or when handling the treated animal. In order to avoid contact, disposable protective gloves obtained with this product at the point of sale must be worn when handling and administering the product.
If skin contact does occur, wash the affected area immediately with soap and water. In some cases, soap and water is not sufficient to remove the product spilled on the fingers, therefore gloves must be used.
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 product packaging.
This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.
The 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 product using paper tissue and clean the area with detergent.
Hypersensitivity reactions to the product have been reported in a small number of people. The product should not be used by persons with a hypersensitivity to the active substance or to any of the excipients (see contraindications, section 4.3). 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.

4.6 Adverse reactions (frequency and seriousness)

Mild and transient skin reactions at the application site, such as erythema and pruritus or alopecia were commonly observed in clinical trials (2.2% of treated cats).

The following other signs shortly after administration were uncommonly observed:
apathy/tremors/anorexia (0.9% of treated cats) or vomiting/hypersalivation (0.4% of treated cats).

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

4.7 Use during pregnancy, lactation or lay

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.

4.8 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 Bravecto spot-on solution for cats and routinely used veterinary medicinal products were observed.

4.9 Amounts to be administered and administration route

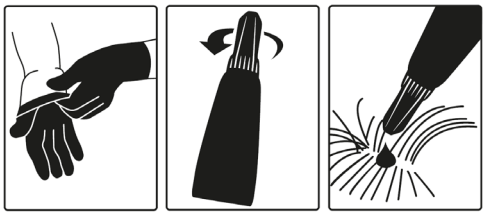
For spot-on use.

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

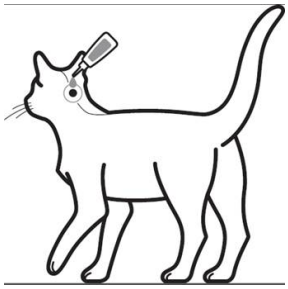
Bodyweight of cat (kg)	**Strength and number of pipettes to be administered**		
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg
1.2 – 2.8	1		
>2.8 – 6.25		1	
>6.25 – 12.5			1

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

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 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 bodyweight.

Treatment schedule
For optimal control of tick and flea infestation, the product should be administered at intervals of 12 weeks.

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

No adverse reactions were observed following topical administration to kitten aged 11-13 weeks and weighing 1.2-1.5 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 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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Ectoparasiticides for systemic use
ATCvet code: QP53B E02

5.1 Pharmacodynamic properties

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes* spp.) and fleas (*Ctenocephalides* spp.) 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 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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dimethylacetamide
Glycofurol
Diethyltoluamide (DEET)
Acetone

6.2 Major incompatibilities

None known.

6.3 Shelf life

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

6.4. 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 immediateley prior to use.

6.5 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.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. 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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11/02/2014

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Chewable tablets:
Intervet GesmbH
Siemensstrasse 107
1210 Vienna
AUSTRIA

Spot-on solution:
Intervet Productions
Rue de Lyons
27460 Igoville
FRANCE

Intervet UK Limited
Walton Manor, Walton,
Milton Keynes,
Buckinghamshire, MK7 7AJ
UNITED KINGDOM

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard 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)
fluralaner

2. STATEMENT OF ACTIVE SUBSTANCES

Fluralaner 112.5 mg
Fluralaner 250 mg
Fluralaner 500 mg
Fluralaner 1,000 mg
Fluralaner 1,400 mg

3. PHARMACEUTICAL FORM

Chewable tablet

4. PACKAGE SIZE

1 chewable tablet
2 chewable tablets
4 chewable tablets

5. TARGET SPECIES

Dog

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

8. WITHDRAWAL PERIOD(S)

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP: {month/year}

11. SPECIAL STORAGE CONDITIONS

Read the package leaflet before use.

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

Read the package leaflet before use.

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

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/13/158/001
EU/2/13/158/002
EU/2/13/158/003
EU/2/13/158/004
EU/2/13/158/005
EU/2/13/158/006
EU/2/13/158/007
EU/2/13/158/008
EU/2/13/158/009
EU/2/13/158/010
EU/2/13/158/011
EU/2/13/158/012
EU/2/13/158/013

EU/2/13/158/014
EU/2/13/158/015

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

3. EXPIRY DATE

EXP: (MM/YYYY)

4. BATCH NUMBER

Lot: {number}

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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)
fluralaner

2. STATEMENT OF ACTIVE SUBSTANCES

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

3. PHARMACEUTICAL FORM

Spot-on solution

4. 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

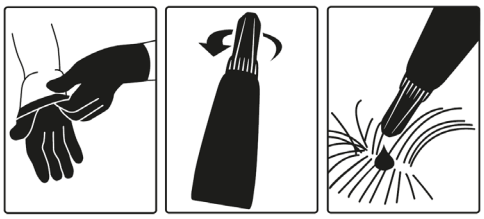
5. TARGET SPECIES

Dogs

6. INDICATIONS

7. METHOD AND ROUTE OF ADMINISTRATION

Spot-on use.
Read the package leaflet before use.
Cap does not come off.



8. WITHDRAWAL PERIOD(S)

Not applicable

9. SPECIAL WARNING(S), IF NECESSARY

Keep the product in the original packaging until use in order to prevent children from getting access to the 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 product. Read package leaflet for full user safety information.

10. EXPIRY DATE

EXP: {month/year}

11. SPECIAL STORAGE CONDITIONS

Read the package leaflet before use.

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

Read the package leaflet before use.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

16. MARKETING AUTHORISATION NUMBER(S)

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)

17. MANUFACTURER'S BATCH NUMBER

Lot:{number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

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)
fluralaner

2. QUANTITY OF THE ACTIVE SUBSTANCE

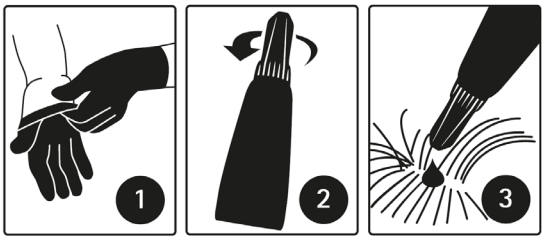
112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner
1,000 mg fluralaner
1,400 mg fluralaner

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

0.4 ml
0.89 ml
1.79 ml
3.57 ml
5.0 ml

4. ROUTE 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 PERIOD(S)

Not applicable

6. BATCH NUMBER

Lot:{number}

7. EXPIRY DATE

EXP: {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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)
fluralaner

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner

3. PHARMACEUTICAL FORM

Spot-on solution

4. 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

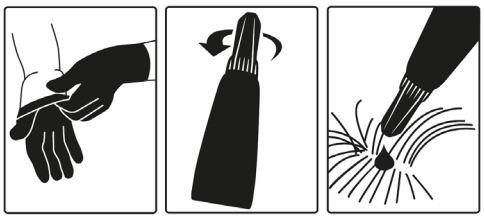
5. TARGET SPECIES

Cats

6. INDICATIONS

7. METHOD AND ROUTE OF ADMINISTRATION

Spot-on use.
Read the package leaflet before use.
Cap does not come off.



8. WITHDRAWAL PERIOD(S)

Not applicable

9. SPECIAL WARNING(S), IF NECESSARY

Keep the product in the original packaging until use in order to prevent children from getting access to the 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 product. Read package leaflet for full user safety information.

10. EXPIRY DATE

EXP: {month/year}

11. SPECIAL STORAGE CONDITIONS

Read the package leaflet before use.

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

Read the package leaflet before use.

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

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

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)

17. MANUFACTURER'S BATCH NUMBER

Lot:{number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

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)
fluralaner

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

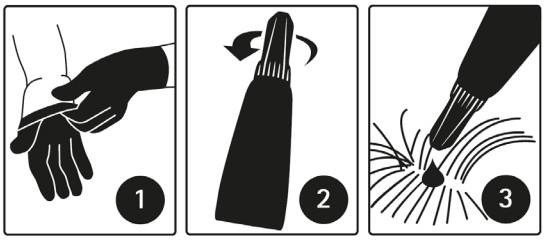
112.5 mg fluralaner
250 mg fluralaner
500 mg fluralaner

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

0.4 ml
0.89 ml
1.79 ml

4. ROUTE 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 PERIOD(S)

Not applicable

6. BATCH NUMBER

Lot:{number}

7. EXPIRY DATE

EXP: {month/year}

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
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)

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

Marketing authorisation holder:
Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The NETHERLANDS

Manufacturer responsible for batch release:
Intervet GesmbH
Siemensstrasse 107
1210 Vienna
AUSTRIA

2. 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)

fluralaner

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Each chewable tablet of Bravecto 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.

4. INDICATIONS

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*.

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance. The onset of effect is within 8 hours of attachment for fleas (*C. felis*) and 12 hours of attachment for ticks (*I. ricinus*).

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

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Mild and transient gastrointestinal effects such as diarrhoea, vomiting, inappetence, and drooling were commonly observed in clinical trials (1.6% of treated dogs).

Convulsions and lethargy has been reported very rarely in spontaneous (pharmacovigilance) reports.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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

7. TARGET SPECIES

Dogs

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

For oral use.

Bravecto chewable tablets 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		

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
>20 -40				1	
>40 - 56					1

For dogs above 56 kg bodyweight, use a combination of two tablets that most closely matches the bodyweight.

9. ADVICE ON CORRECT ADMINISTRATION

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

Bravecto is a chewable tablet and 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 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 4.

10. WITHDRAWAL PERIOD(S)

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 WARNINGS

Special warnings for each target species:
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.

Special precautions for use in animals:
Use with caution in dogs with pre-existing epilepsy.
In the absence of available data, the product should not be used on puppies less than 8 weeks old and /or dogs weighing less than 2 kg.
The 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 product in the original packaging until use, in order to prevent children from getting direct access to the product.

Do not eat, drink or smoke while handling the product.
Wash hands thoroughly with soap and water immediately after use of the 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:
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 clinical field testing, no interactions between Bravecto chewable tablets for dogs and routinely used veterinary medicinal products were observed.

Overdose (symptoms, emergency procedures, antidotes):
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:
None known.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

15. OTHER INFORMATION

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

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.

PACKAGE LEAFLET:
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)

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

Marketing authorisation holder:
Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer responsible for batch release:
Intervet Productions
Rue de Lyons
27460 Igoville
FRANCE

Intervet UK Limited
Walton Manor, Walton,
Milton Keynes,
Buckinghamshire, MK7 7AJ
United Kingdom

2. 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)
fluralaner

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENT(S)

Each ml contains 280 mg fluralaner.
Each pipette delivers:

	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.

4. INDICATIONS

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

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Mild and transient skin reactions at the application site such as erythema or alopecia were commonly observed in clinical trials (1.2% of treated dogs).

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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

7. TARGET SPECIES

Dogs.

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

For spot-on use.
Bravecto should be administered in accordance with the following table (corresponding to a dose of 25-56 mg fluralaner/kg body weight):

Bodyweight 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		

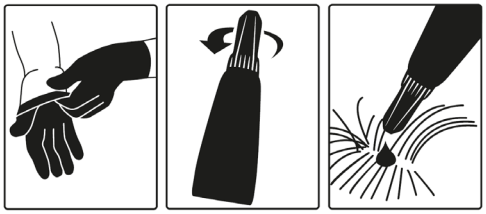
Bodyweight of dog (kg)	Strength and number of pipettes to be administered				
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg	Bravecto 1,000 mg	Bravecto 1,400 mg
>20 - 40				1	
>40 - 56					1

For dogs above 56 kg body weight, use a combination of two pipettes that most closely matches the body weight.

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 optimal control of tick and flea infestation, the product should be administered at intervals of 12 weeks.

10. WITHDRAWAL PERIOD(S)

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 WARNINGS

Special warnings for each target species:
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.

Special precautions for use in animals
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 product should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
This 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
This product is harmful after ingestion. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the 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 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. Contact may occur either directly, when handling the product, or when handling the treated animal. In order to avoid contact, disposable protective gloves obtained with this product at the point of sale must be worn when handling and administering the product.
If skin contact does occur, wash the affected area immediately with soap and water. In some cases, soap and water is not sufficient to remove the product spilled on the fingers, therefore gloves must be used.
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 product packaging.
This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.
The 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 product using paper tissue and clean the area with detergent.
Hypersensitivity reactions to the product have been reported in a small number of people. The product should not be used by persons with a hypersensitivity to the active substance or to any of the excipients (see section Contraindications). 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.

Pregnancy, 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 Bravecto spot-on solution for dogs 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.

Incompatibilities:
None known.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

The 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*).
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.
Not all pack sizes may be marketed.

PACKAGE LEAFLET:
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)

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

Marketing authorisation holder:
Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer responsible for batch release:
Intervet Productions
Rue de Lyons
27460 Igoville
FRANCE

Intervet UK Limited
Walton Manor, Walton,
Milton Keynes,
Buckinghamshire, MK7 7AJ
United Kingdom

2. 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)
fluralaner

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains 280 mg fluralaner.
Each pipette delivers:

	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.

4. INDICATIONS

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

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Mild and transient skin reactions at the application site, such as erythema and pruritus or alopecia were commonly observed in clinical trials (2.2% of treated cats).
The following other signs shortly after administration were uncommonly observed:
apathy/tremors/anorexia (0.9% of treated cats) or vomiting/hypersalivation (0.4% of treated cats).

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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

7. TARGET SPECIES

Cats.

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

For spot-on use.

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

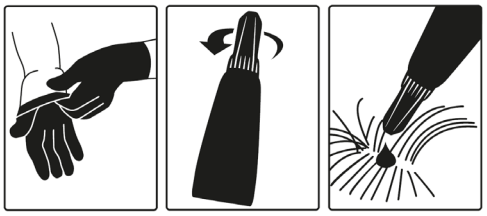
Bodyweight of cat (kg)	**Strength and number of pipettes to be administered**		
	Bravecto 112.5 mg	Bravecto 250 mg	Bravecto 500 mg
1.2 – 2.8	1		
>2.8 – 6.25		1	
>6.25 – 12.5			1

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

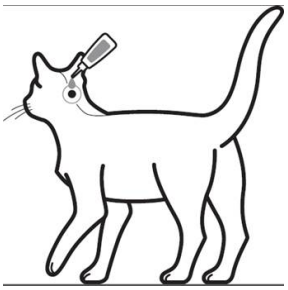
9. ADVICE ON CORRECT ADMINISTRATION

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 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 bodyweight.

Treatment schedule

For optimal control of tick and flea infestation, the product should be administered at intervals of 12 weeks.

10. WITHDRAWAL PERIOD(S)

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 immediateley 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 WARNINGS

Special warnings for each target species:

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.

Special precautions for use in animals

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 kitten less than 11 weeks old and /or cats weighing less than 1.2 kg.
The product should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
This 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

This product is harmful after ingestion. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the 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 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. Contact may occur either directly, when handling the product, or when handling the treated animal. In order to avoid contact, disposable protective gloves obtained with this product at the point of sale must be worn when handling and administering the product.
If skin contact does occur, wash the affected area immediately with soap and water. In some cases, soap and water is not sufficient to remove the product spilled on the fingers, therefore gloves must be used.
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 product packaging.
This product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.
The 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 product using paper tissue and clean the area with detergent.
Hypersensitivity reactions to the product have been reported in a small number of people. The product should not be used by persons with a hypersensitivity to the active substance or to any of the excipients (see section Contraindications). 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.

Pregnancy, 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 Bravecto spot-on solution for cats and routinely used veterinary medicinal products were observed.

Overdose:
Safety was demonstrated in kitten aged 11-13 weeks and weighing 1.2-1.5 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 product at the maximum recommended dose was well tolerated in cats, apart from some self-limiting salivation and coughing or vomiting immediately after administration.

Incompatibilities:
None known.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

15. OTHER INFORMATION

The 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*).
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.
Not all pack sizes may be marketed.

ANNEX IV

GROUNDS FOR ONE ADDITIONAL RENEWAL

The MAH and the CVMP previously agreed to conduct enhanced monitoring of certain categories of serious adverse events in order to obtain increased detail regarding those adverse events. Additionally, in view of the outstanding pharmacovigilance data that were undergoing evaluation at the time of the renewal procedure and to ensure that the MAH's pharmacovigilance system is adequate to enable collection and evaluation of adverse events in line with the requirements; the CVMP at their meeting on 4-6 December 2018 decided that one additional five-year renewal is required.