

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto Plus 112.5 mg / 5.6 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto Plus 500 mg / 25 mg spot-on solution for large cats (>6.25 – 12.5 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each ml of solution contains 280 mg fluralaner and 14 mg moxidectin.

Each pipette delivers:

BRAVECTO PLUS spot-on solution	Pipette content (ml)	Fluralaner (mg)	Moxidectin (mg)
for small cats 1.2 – 2.8 kg	0.4	112.5	5.6
for medium-sized cats >2.8 – 6.25 kg	0.89	250	12.5
for large cats >6.25 – 12.5 kg	1.79	500	25

Excipient(s):

Butylhydroxytoluene 1.07 mg/ml

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 cats with, or at risk from, mixed parasitic infestations by ticks or fleas and ear mites, gastrointestinal nematodes or heartworm. The veterinary medicinal product is exclusively indicated when use against ticks or fleas and one or more of the other target parasites is indicated at the same time.

For the treatment of tick and flea infestations in cats providing 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 flea allergy dermatitis (FAD).

For the treatment of infestations with ear mites (*Otodectes cynotis*).

For the treatment of infections with intestinal roundworm (4th stage larvae, immature adults and adults of *Toxocara cati*) and hookworm (4th stage larvae, immature adults and adults of *Ancylostoma tubaeforme*).

When administered repeatedly at a 12-week interval, the product continuously prevents heartworm disease caused by *Dirofilaria immitis* (see details in section 4.9).

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

Ticks and fleas 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.

Cats in areas endemic for heartworm (or those which have travelled to endemic areas) may be infected with adult heartworms. No therapeutic effect against adult *Dirofilaria immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that animals of 6 months of age or older and living in areas where a vector exists, should be tested for existing adult heartworm infections before application of the veterinary medicinal product for the prevention of heartworm disease.

For the prevention of heartworm disease in cats that are only temporarily in endemic areas, the product should be applied before the first expected exposure to mosquitoes and should be continued at 12-week intervals until return to a non-endemic area. The period between treatment and return from the endemic areas should not exceed 60 days.

For the treatment of infections with ear mites (*Otodectes cynotis*) or the gastrointestinal nematodes *T. cati* and *A. tubaeforme*, the need for, and the frequency of, re-treatment as well as the choice of the treatment (monosubstance or combination product) should be evaluated by the prescribing veterinarian.

Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class under specific circumstances. The use of this veterinary medicinal product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance. Parasite control is recommended throughout the period of potential infestation risk.

Avoid frequent swimming or shampooing the animal because the maintenance of effectiveness of the product in these cases has not been tested.

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, treatment of kittens less than 9 weeks of age and cats less than 1.2 kg bodyweight is not recommended.

Treatment of male breeding animals is not recommended.

This product is for topical use and should not be administered orally.

Oral uptake of the product at the maximum recommended dose of 93 mg fluralaner + 4.65 mg moxidectin/kg body weight induced some self-limiting salivation or single incidences of vomiting immediately after administration.

It is important to apply the dose as indicated to prevent the animal from licking and ingesting the product.

Do not allow recently treated animals to groom each other.

Do not allow treated animals to come into contact with untreated animals until the application site is dry.

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

Contact with the product should be avoided and disposable protective gloves obtained with this product at the point of sale must be worn when handling the 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 product.

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.

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 product spilled on the fingers.

Contact with the 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 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 product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.

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 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.

4.6 Adverse reactions (frequency and seriousness)

Mild and transient skin reactions at the application site (alopecia, flaking skin, redness and pruritus) were commonly observed in clinical trials.

The following other adverse reactions were uncommonly observed in clinical trials shortly after administration: dyspnoea after licking the application site, hypersalivation, emesis, haematemesis, diarrhoea, lethargy, pyrexia, tachypnoea, mydriasis.

Tremors and anorexia have been reported very rarely after the use of this product based on post marketing safety experience (pharmacovigilance).

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 in pregnant or lactating animals and therefore use in such animals is not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

Macrocyclic lactones including moxidectin have been shown to be substrates for p-glycoprotein. Therefore, during treatment with Bravecto Plus, other products that can inhibit p-glycoprotein (e.g. cyclosporine, ketoconazole, spinosad, verapamil) should only be used concomitantly according to the benefit-risk assessment of the responsible veterinarian.

4.9 Amounts to be administered and administration route

For spot-on use.

Bravecto Plus spot-on solution is available in three pipette sizes. The following table defines the size of pipette to be used according to the body weight of the cat (corresponding to a dose of 40-94 mg fluralaner/kg body weight and 2-4.7 mg moxidectin/kg body weight):

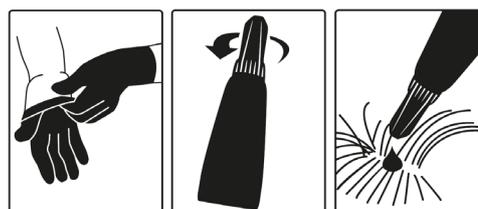
Weight of cat (kg)	Pipette size to be used
1.2 – 2.8	Bravecto Plus 112.5 mg + 5.6 mg spot-on solution for small cats
>2.8 – 6.25	Bravecto Plus 250 mg + 12.5 mg spot-on solution for medium-sized cats
>6.25 – 12.5	Bravecto Plus 500 mg + 25 mg spot-on solution for large cats

Within each weight band, the content of one whole pipette should be used.

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

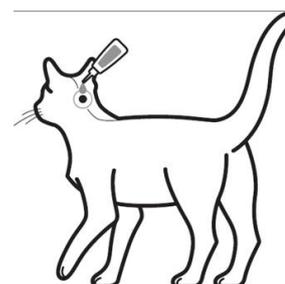
Method of administration

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 at the base of the skull on cats greater than 6.25 kg bodyweight.



Treatment

For the concurrent treatment of infections with ear mites (*Otodectes cynotis*), a single dose of the product should be applied. Seek further veterinary examination (i.e. otoscopy) 28 days after treatment to determine whether there is re-infestation requiring additional treatment. The choice of the additional treatment (monosubstance or combination product) should be determined by the prescribing veterinarian.

For the concurrent treatment of infections with the gastrointestinal nematodes *T. cati* and *A. tubaeforme*, a single dose of the product should be applied. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian and take into account the local epidemiological situation.

Where necessary, cats can be re-treated at 12-week intervals.

Cats in areas endemic for heartworm, or cats which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to application of Bravecto Plus for the concurrent prevention of infection with adult *D. immitis*, the advice provided in section 4.4 should be considered.

At the time of treatment, the product is effective against *D. immitis* larvae (L3 and L4), which have infected the cat in the previous 30 days.

The product is effective against incoming *D. immitis* larvae (L3) for 60 days after treatment.

Therefore, for continuous prevention of heartworm disease cats need to be retreated at 12-week intervals.

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

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 fluralaner + 4.65 mg moxidectin, 279 mg fluralaner + 13.95 mg moxidectin and 465 mg fluralaner + 23.25 mg moxidectin/kg body weight) on three occasions at shorter intervals than recommended (8-week intervals).

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, insecticides and repellents, endectocides, milbemycins.

ATCvet code: QP54AB52.

5.1 Pharmacodynamic properties

Fluralaner

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*Ixodes ricinus*), fleas (*Ctenocephalides felis*) and ear mites (*Otodectes cynotis*) on the cat.

The onset of effect (killing effect) for ticks (*I. ricinus*) and fleas (*C. felis*) is within 48 hours 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), cyclodienes (tick, flea), phenylpyrazoles (tick, flea), benzophenyl ureas (tick), and pyrethroids (tick).

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.

Moxidectin

Moxidectin, a semisynthetic derivative of nemadectin, belongs to the milbemycin group of macrocyclic lactones (avermectins being the other) and has parasitocidal activity against a range of internal and external parasites (including ear mites (*Otodectes cynotis*)). Moxidectin lacks substantial efficacy against fleas and ticks. Moxidectin is only active on larvae (L3 and L4) of *Dirofilaria immitis* and not on adult worms. The effect on *Dirofilaria immitis* larvae has been shown to last over a period of 60 days after treatment with the product and on *D. immitis* larvae that infected the host up to 30 days before treatment.

Milbemycins and avermectins have a common mode of action that is based on the binding of ligand-gated chloride channels (glutamate-R and GABA-R). This leads to an increased membrane permeability of nematode and arthropod nerve and/or muscle cells for chloride ions and results in hyperpolarization, paralysis and death of the parasites. Binding of glutamate-gated chloride channels, which are specific to invertebrates and do not exist in mammals, is considered the main mechanism for the anthelmintic and insecticidal activity.

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. Fluralaner is slowly eliminated from plasma ($t_{1/2} = 15$ days) and excreted in faeces and to a very low extent in urine.

Moxidectin is readily systemically absorbed from the topical administration site, reaching maximum concentrations in plasma between 1 and 5 days after administration. Moxidectin is slowly eliminated from plasma ($t_{1/2} = 26$ days) and excreted in faeces and to a very low extent in urine.

The pharmacokinetic profiles of fluralaner and moxidectin are not affected by co-administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene
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:

Bravecto Plus 112.5 mg / 5.6 mg spot-on solution: 2 years

Bravecto Plus 250 mg / 12.5 mg and 500 mg / 25 mg spot-on solution: 3 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 sachets 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 a high-density polyethylene (HDPE) cap and packed in a laminated aluminium foil sachet.

Each cardboard box contains 1 or 2 pipettes and a pair of gloves per pipette. 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.

Do not allow the product to enter water courses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/18/224/001-006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08/05/2018

10 DATE OF REVISION OF THE TEXT

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(s) responsible for batch release

Intervet Productions
Rue de Lyons
27460 Igoville
FRANCE

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 Plus 112.5 mg / 5.6 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto Plus 500 mg / 25 mg spot-on solution for large cats (>6.25 – 12.5 kg)
fluralaner / moxidectin

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg fluralaner / 5.6 mg moxidectin
250 mg fluralaner / 12.5 mg moxidectin
500 mg fluralaner / 25 mg moxidectin

3. PHARMACEUTICAL FORM

Spot-on solution

4. PACKAGE SIZE

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

5. TARGET SPECIES

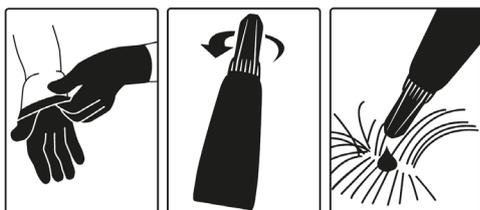
Cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) 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 sachet 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/2/18/224/001 (112.5 mg + 5.6 mg, 1 pipette)
EU/2/18/224/002 (112.5 mg + 5.6 mg, 2 pipettes)
EU/2/18/224/003 (250 mg + 12.5 mg, 1 pipette)
EU/2/18/224/004 (250 mg + 12.5 mg, 2 pipettes)
EU/2/18/224/005 (500 mg + 25 mg, 1 pipette)
EU/2/18/224/006 (500 mg + 25 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 Plus 112.5 mg / 5.6 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto Plus 500 mg / 25 mg spot-on solution for large cats (>6.25 – 12.5 kg)
fluralaner / moxidectin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

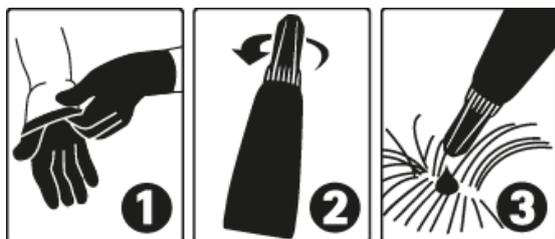
112.5 mg fluralaner / 5.6 mg moxidectin
250 mg fluralaner / 12.5 mg moxidectin
500 mg fluralaner / 25 mg moxidectin

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

0.4 ml
0.89 ml
1.79 ml

4. ROUTE(S) 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.



MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto Plus

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

112.5 mg fluralaner / 5.6 mg moxidectin
250 mg fluralaner / 12.5 mg moxidectin
500 mg fluralaner / 25 mg moxidectin

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

0.4 ml
0.89 ml
1.79 ml

4. ROUTE(S) OF ADMINISTRATION



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 Plus 112.5 mg / 5.6 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto Plus 500 mg / 25 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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto Plus 112.5 mg / 5.6 mg spot-on solution for small cats (1.2 – 2.8 kg)
Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)
Bravecto Plus 500 mg / 25 mg spot-on solution for large cats (>6.25 – 12.5 kg)
Fluralaner / moxidectin

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

Each ml of solution contains 280 mg fluralaner and 14 mg moxidectin.
Each pipette delivers:

BRAVECTO PLUS spot-on solution	Pipette content (ml)	Fluralaner (mg)	Moxidectin (mg)
for small cats 1.2 – 2.8kg	0.4	112.5	5.6
for medium-sized cats >2.8 – 6.25 kg	0.89	250	12.5
for large cats >6.25 – 12.5 kg	1.79	500	25

Excipient(s):

Butylhydroxytoluene 1.07 mg/ml

Clear colourless to yellow solution.

4. INDICATION(S)

For cats with, or at risk from, mixed parasitic infestations by ticks or fleas and ear mites, gastrointestinal nematodes or heartworm. The veterinary medicinal product is exclusively indicated when use against ticks or fleas and one or more of the other target parasites is indicated at the same time.

For the treatment of tick and flea infestations in cats providing 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 flea allergy dermatitis (FAD).

For the treatment of infestations with ear mites (*Otodectes cynotis*).

For the treatment of infections with intestinal roundworm (4th stage larvae, immature adults and adults of *Toxocara cati*) and hookworm (4th stage larvae, immature adults and adults of *Ancylostoma tubaeforme*).

When administered repeatedly at a 12-week interval, the product continuously prevents heartworm disease caused by *Dirofilaria immitis*.

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 (alopecia, flaking skin, redness and pruritus) were commonly observed in clinical trials.

The following other adverse reactions were uncommonly observed in clinical trials shortly after administration: dyspnoea after licking the application site, hypersalivation, emesis, haematemesis, diarrhoea, lethargy, pyrexia, tachypnoea, mydriasis.

Tremors and anorexia have been reported very rarely after the use of this product based on post marketing safety experience (pharmacovigilance).

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

Cats.

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

For spot-on use.

Bravecto Plus spot-on solution is available in three pipette sizes. The following table defines the size of pipette to be used according to the body weight of the cat (corresponding to a dose of 40-94 mg fluralaner/kg body weight and 2-4.7 mg moxidectin/kg body weight):

Weight of cat (kg)	Pipette size to be used
1.2 – 2.8	Bravecto Plus 112.5 mg + 5.6 mg spot-on solution for small cats
>2.8 – 6.25	Bravecto Plus 250 mg + 12.5 mg spot-on solution for medium-sized cats
>6.25 – 12.5	Bravecto Plus 500 mg + 25 mg spot-on solution for large cats

Within each weight band, the content of one whole pipette should be used.

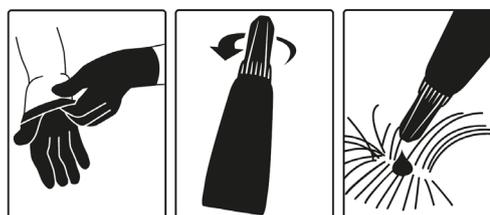
For cats more than 12.5 kg, use a combination of two pipettes that most closely matches the body weight.

9. ADVICE ON CORRECT ADMINISTRATION

Spot-on use.

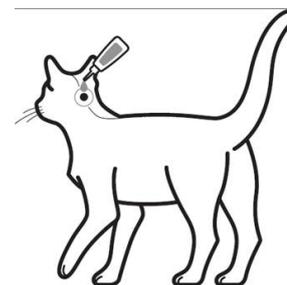
Method of administration

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 at the base of the skull on cats greater than 6.25 kg bodyweight.



Treatment

For the concurrent treatment of infections with ear mites (*Otodectes cynotis*), a single dose of the product should be applied. Seek further veterinary examination (i.e. otoscopy) 28 days after treatment to determine whether there is re-infestation requiring additional treatment. The choice of the additional treatment (monosubstance or combination product) should be determined by the prescribing veterinarian.

For the concurrent treatment of infections with the gastrointestinal nematodes *T. cati* and *A. tubaeforme*, a single dose of the product should be applied. The need for and frequency of re-treatment should be in accordance with the advice of the prescribing veterinarian and take into account the local epidemiological situation.

Where necessary, cats can be re-treated at 12-week intervals.

Cats in areas endemic for heartworm, or cats which have travelled to endemic areas, may be infected with adult heartworms. Therefore prior to application of Bravecto Plus for the concurrent prevention of infection with adult *D. immitis*, the advice provided in section 12 should be considered.

At the time of treatment, the product is effective against *D. immitis* larvae (L3 and L4), which have infected the cat in the previous 30 days.

The product is effective against incoming *D. immitis* larvae (L3) for 60 days after treatment.

Therefore, for continuous prevention of heartworm disease cats need to be retreated at 12-week intervals.

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 sachet 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 WARNING(S)

Special warnings for each target species:

Ticks and fleas 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.

Cats in areas endemic for heartworm (or those which have travelled to endemic areas) may be infected with adult heartworms. No therapeutic effect against adult *Dirofilaria immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that animals of 6 months of age or older and living in areas where a vector exists, should be tested for existing adult heartworm infections before application of the veterinary medicinal product for the prevention of heartworm disease.

For the prevention of heartworm disease in cats that are only temporarily in endemic areas, the product should be applied before the first expected exposure to mosquitoes and should be continued at 12-week intervals until return to a non-endemic area. The period between treatment and return from the endemic areas should not exceed 60 days.

For the treatment of infections with ear mites (*Otodectes cynotis*) or the gastrointestinal nematodes *T. cati* and *A. tubaeforme*, the need for, and the frequency of, re-treatment as well as the choice of the treatment (monosubstance or combination product) should be evaluated by the prescribing veterinarian.

Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class under specific circumstances. The use of this veterinary medicinal product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance. Parasite control is recommended throughout the period of potential infestation risk.

Avoid frequent swimming or shampooing the animal because the maintenance of effectiveness of the product in these cases has not been tested.

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, treatment of kittens less than 9 weeks of age and cats less than 1.2 kg bodyweight is not recommended.

Treatment of male breeding animals is not recommended.

This product is for topical use and should not be administered orally.

Oral uptake of the product at the maximum recommended dose of 93 mg fluralaner + 4.65 mg moxidectin/kg body weight induced some self-limiting salivation or single incidences of vomiting immediately after administration.

It is important to apply the dose as indicated to prevent the animal from licking and ingesting the product.

Do not allow recently treated animals to groom each other.

Do not allow treated animals to come into contact with untreated animals until the application site is dry.

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

Contact with the product should be avoided and disposable protective gloves obtained with this product at the point of sale must be worn when handling the 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 product.

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.

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 product spilled on the fingers.

Contact with the 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 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 product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.

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 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.

Pregnancy, lactation and fertility:

The safety of the veterinary medicinal product has not been established in pregnant or lactating animals and therefore use in such animals is not recommended.

Interaction with other medicinal products and other forms of interaction:

Macrocyclic lactones including moxidectin have been shown to be substrates for p-glycoprotein.

Therefore, during treatment with Bravecto Plus, other products that can inhibit p-glycoprotein (e.g. cyclosporine, ketoconazole, spinosad, verapamil) should only be used concomitantly according to the benefit-risk assessment of the responsible veterinarian.

Overdose (symptoms, emergency procedures, 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 fluralaner + 4.65 mg moxidectin, 279 mg fluralaner + 13.95 mg moxidectin and 465 mg fluralaner + 23.25 mg moxidectin/kg body weight) on three occasions at shorter intervals than recommended (8-week intervals).

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.

Do not allow the product to enter water courses as this may be dangerous for fish and other aquatic organisms.

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 effect (killing effect) for ticks (*I. ricinus*) and fleas (*C. felis*) is within 48 hours after treatment.

Unit dose pipette made of laminated aluminium/polypropylene foil closed with a high-density polyethylene (HDPE) cap and packed in a laminated aluminium foil sachet. Each cardboard box contains 1 or 2 pipettes and a pair of gloves per pipette.

Not all pack sizes may be marketed.