SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravecto Plus 250 mg / 12.5 mg spot-on solution for medium-sized cats (>2.8 – 6.25 kg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:
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 medium-sized cats >2.8 – 6.25 kg	0.89	250	12.5

Excipients:
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, heartworm or lungworm. The veterinary medicinal product is only 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 veterinary medicinal 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 veterinary medicinal product continuously prevents heartworm disease caused by *Dirofilaria immitis* (see details in section 4.9).

Prevention of aelurostrongylosis (by preventing the establishment of adult *Aelurostrongylus abstrusus* responsible for clinical disease).

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

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 veterinary medicinal 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.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the veterinary medicinal product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.
Parasite resistance to any particular class of anthelmintic may develop following frequent, repeated use of an anthelmintic of that class under specific circumstances. Parasite control is recommended throughout the period of potential infestation risk.

The possibility that other animals in the same household can be a source of re-infection with fleas, ear mites or gastrointestinal nematodes should be considered,

and these should be treated as necessary with an appropriate veterinary medicinal product.

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

No therapeutic effect against adult *A. abstrusus* has been established. For the treatment of pre-existing infections with adult *A. abstrusus*, administration of a product authorised for treatment of adult *A. abstrusus* is required.

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 veterinary medicinal product is for topical use and should not be administered orally.
Oral uptake of the veterinary medicinal 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 veterinary medicinal product (see sections 4.6 and 4.9).
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 veterinary medicinal product should be avoided and disposable protective gloves obtained with this veterinary medicinal product at the point of sale must be worn when handling the veterinary medicinal product for the following reasons:
Hypersensitivity reactions have been reported in a small number of people, which can potentially be serious.
Persons with a hypersensitivity to fluralaner or to any of the excipients should avoid any exposure to the veterinary medicinal product.
The veterinary medicinal product binds to skin and may also bind to surfaces after spillage of the 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 veterinary medicinal product may also occur when handling the treated animal.
Make sure that your animal's application site is no longer noticeable before resuming contact with the site of application. This includes cuddling the animal and sharing a

bed with the animal. It takes up to 48 hours for the application site to become dry but it will be noticeable for longer.
If skin reactions occur, consult a physician and show them the veterinary medicinal product packaging.
People with a sensitive skin or known allergy in general e.g., to other veterinary medicinal products of this type should handle the veterinary medicinal product as well as treated animals with caution.
This veterinary medicinal product can cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.
This veterinary medicinal product is harmful after ingestion. Keep the veterinary medicinal product in the original packaging until use, in order to prevent children from getting direct access to the veterinary medicinal product. A used pipette should immediately be disposed of. In case of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician.
The veterinary medicinal product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition. In case of spillage onto, for example table or floor surfaces, remove excess product using paper tissue and clean the area with detergent.

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

4.6 Adverse reactions (frequency and seriousness)

Cats.

Common (1 to 10 animals / 100 animals treated):	Skin reactions at the application site (application site alopecia, flaking skin, application site reddening and application site pruritus)[#].
Uncommon (1 to 10 animals / 1,000 animals treated):	Dyspnoea (after licking the application site), Tachypnoea; Hypersalivation, Emesis, Haematemesis, Diarrhoea; Lethargy, Pyrexia; Mydriasis.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anorexia; Neurological disorders (e.g. tremor, ataxia).

[#]mild and transient

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

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 the veterinary medicinal product, 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 Amount(s) to be administered and administration route

For spot-on use.

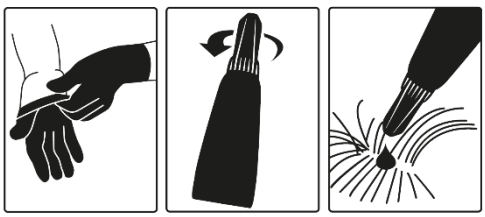
The veterinary medicinal product is available in three pipette sizes. The following table defines the size of pipette to be used according to the body weight of the cat (corresponding to a dose of 40-94 mg fluralaner/kg body weight and 2-4.7 mg moxidectin/kg body weight):

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

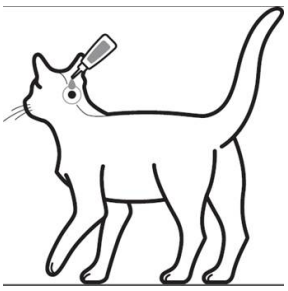
Within each weight band, the content of one whole pipette should be used.
For cats more than 12.5 kg, use a combination of two pipettes that most closely matches the body weight.
Underdosing could result in ineffective use and may favour resistance development.

Method of administration

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



Step 2: The cat should be standing or lying with its back horizontal for easy application. Place the pipette tip on the base of the skull of the cat.



Step 3: Squeeze the pipette gently and apply the entire contents directly to the cat's skin. The veterinary medicinal product should be applied on cats up to 6.25 kg body weight in one spot at the base of the skull and in two spots 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 veterinary medicinal 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 veterinary medicinal product should be applied. The need for and frequency of re-treatment should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

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 the veterinary medicinal product 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 veterinary medicinal 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.

To prevent the establishment of adult lungworms responsible for clinical aelurostrongylosis, 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 parasiticidal activity against a range of internal and external parasites (including ear mites (*Otodectes cynotis*) and lungworm (*Aelurostrongylus abstrusus*)). 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 hyperpolarisation, 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
Acetone

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 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 immediateley 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.
Medicines should not be disposed of via wastewater.
The veterinary medicinal product should not enter water courses as fluralaner and moxidectin may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Limited
Walton Manor, Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

Vm 01708/5028

9. DATE OF FIRST AUTHORISATION

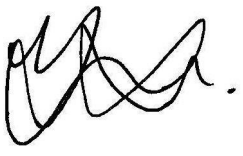
8 May 2018

10. DATE OF REVISION OF THE TEXT

September 2023

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.



Approved: 05 September 2023