FOR EXTERNAL ANIMAL USE ONLY

BRAVECTO® PLUS
Reg. No. G4408 (Act 36/1947)
Namibia Reg. No. V22/18.1.8/1505 NS0

For Small Cats
For Medium Cats
For Large Cats

INDICATIONS

For cats suffering from, or at risk of, mixed ecto- and endoparasitic infestations.

- For the treatment of tick and flea infestations in cats. **Bravecto® Plus** is a systemic insecticide and acaricide that provides immediate and persistent flea (*Ctenocephalides felis*) and tick (*Ixodes ricinus, Ixodes scapularis, Rhipicephalus sanguineus* and *Haemaphysalis* spp.) killing activity for 3 months.
- For the treatment of ear mites (*Otodectes cynotis*) in cats.
- For the prevention of heartworm disease caused by *Dirofilaria immitis* for 3 months.
- For the treatment of infestations of intestinal roundworm (*Toxocara cati*; fourth stage larvae, immature adults and adults) and hookworm (*Ancylostoma tubaeforme*; fourth stage larvae, immature adults and adults).

Fleas and ticks must attach to the host and commence feeding in order to be exposed to the active substance.
Bravecto® Plus can be used as part of a treatment strategy for flea allergy dermatitis (FAD).

CAUTION

STORAGE

- Store at or below 25 °C.
- 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 which is stated on the container label.

COMPOSITION

Each 1 mℓ of **Bravecto® Plus** contains **280 mg fluralaner** and **14 mg moxidectin.**
Each pipette of **Bravecto® Plus** delivers the following:

Bravecto® Plus	**Pipette content (mℓ)**	**Fluralaner (mg)**	**Moxidectin (mg)**
Small cats 1,2 to 2,8 kg	0,4	112,5	5,6
Medium cats > 2,8 to 6,25 kg	0,89	250	12,5
Large cats > 6,25 to 12,5 kg	1,79	500	25

Excipient(s):
Butylhydroxytoluene 1,07 mg/mℓ.

WARNINGS

- Parasites need to start feeding on the host to become exposed to fluralaner; therefore, the risk of the transmission of parasite borne diseases cannot be excluded.
- The use of **Bravecto® Plus** 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.
- The efficacy of **Bravecto® Plus** in controlling tapeworm infestations in cats has not yet been determined.
- Keep Bravecto® Plus in the original packaging until use.
- Dispose of empty containers and unused product according to local waste disposal regulations and do not reuse for any other purpose.
- The safety of **Bravecto® Plus** has not been established during pregnancy and lactation. Use only according to the benefit-risk assessment by the responsible veterinarian.
- KEEP OUT OF REACH OF CHILDREN, UNINFORMED PERSONS AND ANIMALS.
- Although this remedy has been extensively tested under a large variety of conditions, failure thereof may ensue as a result of a wide range of reasons. If this is suspected, seek veterinary advice and notify the registration holder.

PRECAUTIONS

- 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 *D. immitis* has been established. It is therefore recommended, in accordance with good veterinary practice, that all animals 6 months of age or more, living in areas where a vector exists, should be tested for existing adult heartworm infections before beginning preventive use with **Bravecto® Plus**.
- To ensure continuous prevention of heartworm disease, a repetition of treatment is necessary at 3-month intervals. At the time of treatment, **Bravecto® Plus** is effective against *D. immitis* larvae (L3 and L4), which have developed in the previous 30 days and against incoming *D. immitis* larvae (L3 and L4) for the subsequent 60 days.
- Prevention of heartworm disease in cats that are only temporarily in endemic areas, should start at the latest within 1 month after the first expected exposure to mosquitoes and should be continued at 12-week intervals until return to a non-endemic area.
- For the treatment of infestations with the gastrointestinal nematodes *T. cati* and *A. tubaeforme*, the need for, and the frequency of retreatment, 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 **Bravecto® Plus** 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 **Bravecto® Plus** 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 younger than 9 weeks of age and cats less than 1,2 kg body weight should be based on a benefit-risk assessment by the responsible veterinarian.
- Treatment of male breeding animals is not recommended due to an observed decrease in spermatogenesis in male rats during toxicology studies of moxidectin. The impact of **Bravecto® Plus** on mating performance, sperm quality, fertility or offspring data has not been tested in male cats.
- **Bravecto® Plus** should not be administered at intervals shorter than 8 weeks as the safety at shorter intervals has not been tested.
- **Bravecto® Plus** is for topical use and should not be administered orally.
- 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

- **Bravecto® Plus** is harmful after ingestion.
- Keep **Bravecto® Plus** in the original packaging until use, 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.
- This product, and the wet skin of a recently treated animal, may be slightly irritating to the skin and moderately irritating to the eyes.
- Avoid contact with skin, mouth and/or eye, including hand-to-mouth and/or hand-to-eye contact.
- Do not eat, drink or smoke while handling the product.
- Do not come into contact or allow children to come into contact with the application site until it is dry; it is therefore recommended to treat the animal in the evening. On the day of treatment, treated animals should not be permitted to sleep in the same bed as their owner, especially children.
- Wash hands thoroughly with soap and water immediately after use of the product. If skin contact does occur, wash the affected area immediately with water. In some cases, water is not sufficient to remove the product spilled on the fingers. If a sticky residue persists on the skin after washing with water, then this can be removed using household items containing organic solvents [e.g. rubbing alcohol (ethanol, isopropyl alcohol) or nail polish remover (acetone)] applied gently with a swab.
- In case of contact with the eyes, immediately rinse thoroughly with water.
- The product is highly flammable. Keep away from heat, sparks, open flames or other sources of ignition.

DIRECTIONS FOR USE – USE ONLY AS DIRECTED

- For topical spot-on use.
- **Bravecto® Plus** is available in 3 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 to 94 mg fluralaner/kg body weight and 2 to 4,7 mg moxidectin/kg body weight):

Weight of cat (kg)	Pipette size to be used
1,2 to 2,8	**Bravecto® Plus** 112,5 mg & 5,6 mg spot-on solution for small cats
> 2,8 to 6,25	**Bravecto® Plus** 250 mg & 12,5 mg spot-on solution for medium cats
> 6,25 to 12,5	**Bravecto® Plus** 500 mg & 25 mg spot-on solution for large cats

Within each weight band, the content of 1 whole pipette should be used.
For cats more than 12,5 kg, use a combination of 2 pipettes that most closely matches the body weight.

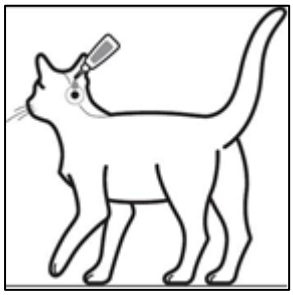
Advice on correct administration

Method of administration

Step 1: Immediately before use, open the sachet and remove the pipette. 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 horizontally during application. Part the fur at the administration site. Place the pipette tip vertically against the skin 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. **Bravecto® Plus** should be applied in 1 spot (cats up to 6,25 kg body weight) or 2 spots (cats weighing more than 6,25 kg body weight). If 2 spots are needed, the first spot should be applied at the base of the skull and the second one between the shoulder blades.
It is important to deliver the solution onto an area that cannot be easily licked by the cat. As cats are fastidious groomers, they may inadvertently ingest product if easily reached. Ingestion may cause adverse reactions and will remove product from the coat. If multiple cats are treated and may mutually groom, it is recommended that cats are separated while product dries.



Treatment schedule

For optimal control of tick and flea infestation and for prevention of heartworm disease, **Bravecto® Plus** should be administered at intervals of 3 months.

In fast growing kittens, it is recommended to re-administer **Bravecto® Plus** after 8 weeks to ensure continuous heartworm prevention.

Cats in areas endemic for heartworm, or those which have travelled to endemic areas, may be infected with adult heartworms. Therefore, prior to treatment with **Bravecto® Plus**, the advice provided under "PRECAUTIONS" should be considered.

For the treatment of infestations with gastrointestinal nematodes, the treatment schedule should be based on veterinary diagnosis and on the local epidemiological situation.

CONTRA-INDICATIONS
Do not use in case of hypersensitivity to any of the active substances or to any of the excipients.

ADVERSE REACTIONS
Mild and transient skin reactions at the application site [alopecia (hair loss), flaking skin and pruritus (itchy skin)] were observed in clinical trials (2,9 % of treated cats).

The following other reactions were uncommonly observed in clinical trials shortly after administration: dyspnoea (difficulty breathing) after licking the application site, hematemesis (bloody vomit), diarrhoea, lethargy, hypersalivation (excess drooling), pyrexia (fever), tachypnoea (rapid breathing), mydriasis (dilated pupils) (0,1 % of treated cats).

Based on post-registration experience decreased appetite, tremors and ataxia have been reported very rarely (less than 1 animal in 10 000 animals treated).

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinarian.

OVERDOSE
No adverse reactions were observed following topical administration to kittens aged 9 to 13 weeks and weighing 0,9 to 1,9 kg treated with overdoses of up to 5 times the maximum recommended dose (93 mg fluralaner and 4,65 mg moxidectin, 279 mg fluralaner and 13,95 mg moxidectin and 465 mg fluralaner and 23,25 mg moxidectin/kg body weight) on 3 occasions at shorter intervals than recommended (8-week intervals).
Oral uptake of the product at the maximum recommended dose of 93 mg fluralaner and 4,65 mg moxidectin/kg body weight was well tolerated in cats, apart from some self-limiting salivation (drooling) or single incidences of vomiting immediately after administration.

NOTES FOR THE VETERINARIAN
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.
The safety of concurrent use of Bravecto® Plus and praziquantel (at a dose of 16,7 mg/kg body weight) has been confirmed.

Pharmacodynamic properties

Fluralaner is an acaricide and insecticide. It is efficacious against ticks (*I. ricinus*, *I. scapularis*, *R. sanguineus* and *H.* spp.), fleas (*C. felis*) and ear mites (*O. cynotis*) in cats. The onset of effect is within 48 hours for ticks (*I. ricinus*) and within 12 hours for fleas (*C. felis*) 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* bioassays, 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).

Bravecto® Plus 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, 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 various nematode species as well as mites, lice, warble and horn flies. Moxidectin lacks substantial efficacy against fleas and ticks. Moxidectin is only active on larvae (L3 and L4) of *D. immitis* and not on adult worms.

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.

PRESENTATION
Clear, colourless to yellow solution presented in unit dose pipettes made of laminated aluminium/ polypropylene foil, closed with high density polyethylene (HDPE) caps and packed in laminated aluminium foil sachets.
Each carton box contains 1 or 2 pipettes in either small, medium or large doses.
Not all pack sizes may be marketed.

REGISTRATION HOLDER
Intervet South Africa (Pty) Ltd.
20 Spartan Road
Spartan
1619, RSA
Tel: +27 (0) 11 923 9300
E-mail: msdahza@msd.com

www.msd-animal-health.co.za

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