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BRAVECTO®

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Merck Animal Health

Fluralaner Topical Solution, 112.5 mg, 250 mg, 500 mg
Veterinary Use Only
DIN 02454912, 02454920, 02454939

DESCRIPTION:

BRAVECTO (Fluralaner Topical Solution) contains 280 mg/mL (28%) of fluralaner. Each tube is formulated to provide a minimum dose of 40 mg/kg body weight.

Non-medicinal ingredients: Dimethylacetamide, Glycofurol, Diethyltoluamide (DEET), Acetone.

THERAPEUTIC CLASSIFICATION:

Antiparasitic

INDICATIONS:

BRAVECTO kills adult fleas and is indicated for the treatment and prevention of flea infestations *(Ctenocephalides felis)* for 12 weeks.
BRAVECTO is also indicated for the treatment and control of tick infestations with *Dermacentor variabilis* (American dog tick) and *Ixodes scapularis* (black-legged tick) for 8 weeks.
BRAVECTO is indicated for cats and kittens 6 months of age and older and weighing 1.2 kg or greater.

DOSAGE AND ADMINISTRATION:

BRAVECTO should be administered topically as a single dose every 12 weeks according to the **Dosage Schedule** below to provide a minimum dose of 40 mg/kg body weight.
BRAVECTO should be administered every 8 weeks in case of exposure to *Dermacentor variabilis* and *Ixodes scapularis* ticks (see **EFFICACY**).

Dosage Schedule

Body Weight Ranges (kg)	Fluralaner content (mg/tube)	Tubes Administered	Package Colour
1.2 - 2.8	112.5	One	Lime
> 2.8 - 6.25	250	One	Dark blue
> 6.25 - 12.5*	500	One	Violet

* Cats over 12.5 kg should be administered the appropriate combination of tubes.

Step 1: Immediately before use, open the pouch and remove the tube.
Put on gloves provided at the point of sale.
Hold the tube at the crimped end with the cap in an upright position (tip up). The cap should be rotated clockwise or counter clockwise one full turn.
DO NOT REMOVE THE CAP.
The cap is designed to stay on the tube for dosing.
The tube is open and ready for application when a “click” is heard or felt.
Step 2: The cat should be standing or lying with its back horizontal during application. Part the fur at the administration site.
Place the tube tip vertically against the skin at the base of the skull of the cat.
Step 3: Squeeze the tube and gently apply the entire contents of BRAVECTO directly to the skin at the base of the skull of the cat.
Avoid applying an excessive amount of solution that could cause some of the solution to run and drip off of the animal.
If a second spot is needed to avoid run off, then apply the second spot slightly below the first spot.

Treatment with BRAVECTO may begin at any time of the year. Due to climate variations across the country, Canada has highly variable distributions and abundance of flea and tick infestations. A comprehensive plan, based on regional risk assessment is recommended to determine an appropriate dosing interval.

CONTRAINDICATIONS:

This product should not be given to cats with known or suspected allergy or intolerance to fluralaner or the non-medicinal ingredients of this product.

CAUTIONS:

Avoid ingestion (see **ANIMAL SAFETY**).
BRAVECTO has not been shown to be effective for 12-weeks duration in kittens less than 6 months of age.
The safety of BRAVECTO has not been established in breeding, pregnant and lactating cats.
Fluralaner is a member of the isoxazoline class. This class has been associated with neurological adverse reactions including tremors, ataxia, and seizures. Neurological adverse reactions have been reported in cats receiving isoxazoline class drugs, even in cats without a history of neurological disorders. Use with caution in cats with a history of neurological disorders.

WARNINGS:

- Keep out of the reach of children.
- **Do not contact or allow children to contact the application site until it is no longer noticeable on the animal’s skin/fur. This includes cuddling 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.**
- This product is very sticky and binds to skin and may also bind to surfaces after spillage of the product.
- **Special precautions should be taken by the person who administers this product.**

Adverse reactions have been reported in a small number of people after skin contact. Avoid contact with skin. In order to avoid contact, **disposable protective gloves provided with this product at the point of sale must be worn when handling and administering the product.** If accidental skin contact occurs, wash the skin thoroughly with soap and water immediately. In some cases, soap and water are not sufficient to remove the product, therefore gloves must be worn. Wash hands after use of the product.

- This product can be harmful if ingested. If accidental ingestion occurs, seek medical advice. In order to prevent children from getting direct access to the product, keep tube(s) in unopened pouch until use. Keep unopened pouches in the original carton between uses. Dispose of used tubes immediately after use.
- Do not eat, drink or smoke while handling the product.
- This product can cause eye irritation. If accidental contact occurs, flush eyes thoroughly with water.
- 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 non-medicinal ingredients (See DESCRIPTION for active substance and list of non-medicinal ingredients).
- The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

ADVERSE REACTIONS:

Although all adverse events are not reported, the following information is based on voluntary post-approval drug experience reporting. It is generally recognized that this results in significant under-reporting. The adverse events listed here reflect reporting and not necessarily causality.

The following adverse events have been reported rarely[1] (reported in at least 1 but not more than 10 animals in 10,000 animals exposed) and very rarely [2] (reported in less than 1 in 10,000 animals exposed) and are listed by body system, in decreasing order of frequency:

Application site disorders: application site hair change [1], application site pruritus[2], application site erythema[2]

Systemic disorders: lethargy[1], anorexia[2]

Digestive tract disorders: vomiting[2], hypersalivation[2], diarrhea[2]

Behavioural disorders: agitation[2]

Neurological disorders: ataxia[2], muscle tremor[2], convulsion/seizure[2]

In a well-controlled U.S. field study, which included a total of 161 households and 311 cats (224 with fluralaner and 87 with a topical active control), all potential adverse reactions were recorded and the most frequently reported are listed in the table below:

Percentage of Cats with Adverse Reactions in the Field Study

Adverse Reaction (AR)	Fluralaner Group: Percent of Cats with the AR During the 105-Day Study (n=224 cats)	Control Group: Percent of Cats with the AR During the 84-Day Study (n=87 cats)
Vomiting	7.6%	6.9%
Pruritus	5.4%	11.5%
Diarrhea	4.9%	1.1%
Alopecia	4.9%	4.6%
Decreased appetite	3.6%	0.0%
Lethargy	3.1%	2.3%
Scabs/Ulcerated Lesions	2.2%	3.4%

In the field study, two cats treated with fluralaner topical solution experienced ataxia. One cat became ataxic with a right head tilt 34 days after the first dose. The cat improved within one week of starting antibiotics. The right head tilt and ataxia, along with lateral recumbency, reoccurred 82 days after administration of the first dose. The cat recovered with antibiotics and was redosed with fluralaner topical solution 92 days after administration of the first dose, with no further abnormalities. A second cat became ataxic 15 days after receiving its first dose and recovered the next day. The cat was redosed with fluralaner topical solution 82 days after administration of the first dose, with no further abnormalities.

In a European field study, two cats from the same household experienced tremors, lethargy and anorexia within one day of administration. The signs resolved in both cats within 48 - 72 hours.

In a European field study conducted in 474 cats receiving topical fluralaner, there were three reports of facial dermatitis in humans after close contact with the application site within 4 days of application. Association with the treatment was not substantiated in two cases and in the third case, close contact occurred before the skin at the application site was dry. Such signs were not reported in the US and European field studies in dogs.

CLINICAL PHARMACOLOGY:

Peak fluralaner concentrations are achieved between 7 and 21 days following topical administration and the elimination half-life ranges between 11 and 13 days. The bioavailability of fluralaner following topical administration is approximately 25%.

MODE OF ACTION:

Fluralaner has a systemic mode of action and belongs to the class of isoxazoline-substituted benzamide derivatives. Fluralaner is an inhibitor of the arthropod nervous system. The mode of action of fluralaner is the antagonism of the ligand-gated chloride channels (gamma-aminobutyric acid (GABA)-receptor and glutamate-receptor).

EFFICACY:

In a well-controlled European laboratory study, BRAVECTO killed 100% of fleas 8 hours after treatment and reduced the numbers of live fleas on cats by > 97.7% within 12 hours after treatment or post-infestation for 12 weeks.

In well-controlled U.S. laboratory studies, BRAVECTO demonstrated > 98.9% effectiveness against *Ixodes scapularis* and > 98.4% effectiveness against *Dermacentor variabilis* 48 hours post-infestation for 8 weeks.

Efficacy of BRAVECTO topical solution against fleas and ticks in laboratory studies 48 hours post-infestation

	Study	% Efficacy*			
		Day 2	Day 30	Day 58	Day 86
Ctenocephalides felis	1	100 (100)	100 (100)	100 (100)	99.5 (99.7)
Dermacentor variabilis	1	99.7 (99.7)	100 (100)	98.4 (98.7)	59.9 (76.8)
	2	100 (100)	100 (100)	100 (100)	85.2 (93.7)
Ixodes scapularis	1	98.9 (99.4)	100 (100)	100 (100)	97.7 (98.6)
	2	100 (100)	100 (100)	100 (100)	83.3 (94.6)

* arithmetic mean (geometric mean). Note: the arithmetic mean was used to assess efficacy.

In a well-controlled U.S. field study, a single dose of BRAVECTO reduced fleas by ≥ 98.6% for 12 weeks. Cats with signs of flea allergy dermatitis showed improvement in erythema, alopecia, papules, scales, crusts, and excoriation as a direct result of eliminating flea infestations.

ANIMAL SAFETY:

Margin of Safety Study: In a margin of safety study, BRAVECTO was administered topically to 11- to 13-week (mean age 12 weeks)-old-kittens at 1, 3, and 5X the maximum labeled dose of 93 mg/kg at three, 8-week intervals. The kittens in the control group (0X) were treated with mineral oil.

There were no clinically-relevant, treatment-related effects on physical examination, body weights, food consumption, clinical pathology (hematology, clinical chemistries, coagulation tests, and urinalysis), gross pathology, histopathology, or organ weights. Cosmetic changes at the application site included matting/clumping/spiking of hair, wetness, or a greasy appearance.

Oral Safety Study: In a safety study, one dose of BRAVECTO topical solution was administered orally to 6- to 7-month-old-kittens at 1X the maximum labeled dose of 93 mg/kg. The kittens in the control group (0X) were administered saline orally. There were no clinically-relevant, treatment-related effects on physical examination, body weights, food consumption, clinical pathology (hematology, clinical chemistries, coagulation tests, and urinalysis), gross pathology, histopathology, or organ weights. All treated kittens experienced salivation and four of six experienced coughing immediately after administration. One treated kitten experienced vomiting 2 hours after administration.

In a well-controlled field study BRAVECTO was used concurrently with other medications, such as vaccines, anthelmintics, antibiotics, steroids and sedatives. No adverse reactions were observed from the concurrent use of BRAVECTO with other medications.

STORAGE CONDITIONS:

Do not store above 30°C. Protect from freezing.

HOW SUPPLIED:

BRAVECTO (Fluralaner Topical Solution) is available in three strengths for use in cats (112.5 mg, 250 mg and 500 mg fluralaner per tube). Each tube is packaged individually in a pouch. Product may be supplied in 1 or 2 tubes per box.

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Version: 21FEB2019

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CPN: 1208290.2