

BRAVECTO®

(fluralaner) Chews

Flavored chews for dogs.

Caution:

Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:

Each chew is formulated to provide a minimum dose of 11.4 mg/lb (25 mg/kg) body weight.

The chemical name of fluralaner is (±)-4-[5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl]-2-methyl-N-[2-oxo-2-(2,2,2-trifluoroethylamino) ethyl]benzamide.

Indications:

Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of tick infestations [*Ixodes scapularis* (black-legged tick), *Dermacentor variabilis* (American dog tick), and *Rhipicephalus sanguineus* (brown dog tick)] for 12 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

Bravecto is also indicated for the treatment and control of *Amblyomma americanum* (lone star tick) infestations for 8 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

Dosage and Administration:

Bravecto should be administered orally as a single dose every 12 weeks according to the **Dosage Schedule** below to provide a minimum dose of 11.4 mg/lb (25 mg/kg) body weight.

Bravecto may be administered every 8 weeks in case of potential exposure to *Amblyomma americanum* ticks (see **Effectiveness**).

Bravecto should be administered with food.

Dosage Schedule

Body Weight Ranges (lb)	Fluralaner Content (mg)	Chews Administered
4.4 – 9.9	112.5	One
>9.9 – 22.0	250	One
>22.0 – 44.0	500	One
>44.0 – 88.0	1000	One
>88.0 – 123.0*	1400	One

*Dogs over 123.0 lb should be administered the appropriate combination of chews

Treatment with Bravecto may begin at any time of the year and can continue year round without interruption.

Contraindications:

There are no known contraindications for the use of the product.

Warnings:

Not for human use. Keep this and all drugs out of the reach of children. 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.

Keep Bravecto in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions:

Fluralaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

Bravecto has not been shown to be effective for 12-weeks duration in puppies less than 6 months of age. Bravecto is not effective against *Amblyomma americanum* ticks beyond 8 weeks after dosing (see **Effectiveness**).

Adverse Reactions:

In a well-controlled U.S. field study, which included 294 dogs (224 dogs were administered Bravecto every 12 weeks and 70 dogs were administered an oral active control every 4 weeks and were provided with a tick collar); there were no serious adverse reactions. All potential adverse reactions were recorded in dogs treated with Bravecto over a 182-day period and in dogs treated with the active control over an 84-day period. The most frequently reported adverse reaction in dogs in the Bravecto and active control groups was vomiting.

Percentage of Dogs with Adverse Reactions in the Field Study

Adverse Reaction (AR)	Bravecto Group: Percentage of Dogs with the AR During the 182-Day Study (n=224 dogs)	Active Control Group: Percentage of Dogs with the AR During the 84-Day Study (n=70 dogs)
Vomiting	7.1	14.3
Decreased Appetite	6.7	0.0
Diarrhea	4.9	2.9
Lethargy	5.4	7.1
Polydipsia	1.8	4.3
Flatulence	1.3	0.0

In a well-controlled laboratory dose confirmation study, one dog developed edema and hyperemia of the upper lips within one hour of receiving Bravecto. The edema improved progressively through the day and had resolved without medical intervention by the next morning.

Post Approval Experience (2019):

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported for dogs are listed in decreasing order of reporting frequency for fluralaner:

Vomiting, lethargy, diarrhea (with and without blood), anorexia, pruritis, polydipsia, seizure, allergic reactions (including hives, swelling, erythema), dermatitis (including crusts, pustules, rash), tremors and ataxia.

Contact Information:

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.FDA.gov/reportanimalae>.

Clinical Pharmacology:

Peak fluralaner concentrations are achieved between 2 hours and 3 days following oral administration, and the elimination half-life ranges between 9.3 to 16.2 days. Quantifiable drug concentrations can be measured (lower than necessary for effectiveness) through 112 days. Due to reduced drug bioavailability in the fasted state, fluralaner should be administered with food.

Mode of Action:

Fluralaner is for systemic use 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).

Effectiveness:

Bravecto began to kill fleas within two hours after administration in a well-controlled laboratory study. In a European laboratory study, Bravecto killed fleas and *Ixodes ricinus* ticks and reduced the numbers of live fleas and *Ixodes ricinus* ticks on dogs by > 98% within 12 hours for 12 weeks. In a well-controlled laboratory study, Bravecto demonstrated 100% effectiveness against adult fleas 48 hours post-infestation for 12 weeks. In well-controlled laboratory studies, Bravecto demonstrated ≥ 93% effectiveness against *Dermacentor variabilis*, *Ixodes scapularis* and *Rhipicephalus sanguineus* ticks 48 hours post-infestation for 12 weeks. Bravecto demonstrated ≥90% effectiveness against *Amblyomma americanum* 72 hours post-infestation for 8 weeks, but failed to demonstrate ≥90% effectiveness beyond 8 weeks.

In a well-controlled U.S. field study, a single dose of Bravecto reduced fleas by ≥ 99.7% for 12 weeks. Dogs with signs of flea allergy dermatitis showed improvement in erythema, alopecia, papules, scales, crusts, and excoriation as a direct result of eliminating flea infestations.

Palatability: In a well-controlled U.S. field study, which included 559 doses administered to 224 dogs, 80.7% of dogs voluntarily consumed Bravecto within 5 minutes, an additional 12.5% voluntarily consumed Bravecto within 5 minutes when offered with food, and 6.8% refused the dose or required forced administration.

Animal Safety:

Margin of Safety Study: In a margin of safety study, Bravecto was administered orally to 8- to 9-week-old puppies at 1, 3, and 5X the maximum label dose of 56 mg/kg at three, 8-week intervals. The dogs in the control group (OX) were untreated.

There were no clinically-relevant, treatment-related effects on physical examinations, body weights, food consumption, clinical pathology (hematology, clinical chemistries, coagulation tests, and urinalysis), gross pathology, histopathology, or organ weights. Diarrhea, mucoid and bloody feces were the most common observations in this study, occurring at a similar incidence in the treated and control groups. Five of the twelve treated dogs that experienced one or more of these signs did so within 6 hours of the first dosing. One dog in the 3X treatment group was observed to be dull, inappetent, with evidence of bloody diarrhea, vomiting, and weight loss beginning five days after the first treatment. One dog in the 1X treatment group vomited food 4 hours following the first treatment.

Reproductive Safety Study: Bravecto was administered orally to intact, reproductively-sound male and female Beagles at a dose of up to 168 mg/kg (equivalent to 3X the maximum label dose) on three to four occasions at 8-week intervals. The dogs in the control group (OX) were untreated.

There were no clinically-relevant, treatment-related effects on the body weights, food consumption, reproductive performance, semen analysis, litter data, gross necropsy (adult dogs) or histopathology findings (adult dogs and puppies). One adult 3X treated dog suffered a seizure during the course of the study (46 days after the third treatment). Abnormal salivation was observed on 17 occasions: in six treated dogs (11 occasions) after dosing and four control dogs (6 occasions).

The following abnormalities were noted in 7 pups from 2 of the 10 dams in only the treated group during gross necropsy examination: limb deformity (4 pups), enlarged heart (2 pups), enlarged spleen (3 pups), and cleft palate (2 pups). During veterinary examination at Week 7, two pups from the control group had inguinal testicles, and two and four pups from the treated group had inguinal and cryptorchid testicles, respectively. No undescended testicles were observed at the time of necropsy (days 50 to 71).

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

Storage Information:

Do not store above 86°F (30°C).

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How Supplied:

Bravecto (fluralaner) is available in five strengths (112.5, 250, 500, 1000, and 1400 mg fluralaner per chew). Each chew is packaged individually into aluminum foil blister packs sealed with a peelable paper backed foil lid stock. Product may be packaged in 1, 2, or 4 chews per package.

Approved by FDA under NADA # 141-426

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Fluralaner (active ingred.) Made in Japan.
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