A portfolio of extraordinary flea and tick protection for up to 12 weeks*

BRAVECTO® (FLURALANER) CHEW OR TOPICAL SOLUTION

9 out of 10 pet parents prefer Bravecto compared to monthly treatments.[4]

Chew for Dogs

- **Easier pet owner adherence**
  - — Nearly 3X longer compliance per dose than monthly treatments[1]
- **Fast-acting efficacy**
  - — Kills 100% of fleas and ticks in 12 hours[2,3]
- **Proven safety**
  - — Clinically proven for breeding, pregnant, and lactating dogs[1]
- **Long-lasting**
  - — Potentially fewer gaps in protection with 12-week dosing period
- **Convenient**
  - — 89% of pet owners prefer Bravecto's easy, convenient administration schedule[4]

CHEW FOR DOGS

References:
1. Bravecto [prescribing information]. Madison, NJ: Merck Animal Health; 2014. **2.** Burgio F, et al. *Parasit Vectors* 2016;9(1):626. **3.** Taenzler J, et al. *Parasit Vectors*. 2014;7:567.
4. Lavan P, et al. *J Vet Sci Technol*. 2017;8:439.

***** Bravecto kills fleas and prevents flea infestations. **Bravecto Chew** and **Bravecto Topical for Dogs** kills ticks (black-legged tick, American dog tick, and brown dog tick) for 12 weeks and also kills lone star ticks for 8 weeks. **Bravecto Topical for Cats** kills ticks (black-legged tick) for 12 weeks and American dog ticks for 8 weeks.

Bravecto is for dogs and cats 6 months of age or older. Bravecto Chew and Bravecto Topical for Dogs is approved for pregnant, breeding and lactating dogs. **Bravecto Chew for Dogs:** Side effects may include vomiting, decreased appetite, diarrhea, lethargy, excessive thirst and flatulence. **Bravecto Topical for Dogs:** Side effects may include vomiting, hair loss, diarrhea, lethargy, decreased appetite, and moist dermatitis/rash. **Bravecto Topical for Cats:** Side effects may include vomiting, itching, diarrhea, hair loss, decreased appetite, lethargy, and scabs/ulcerated lesions.

Topical Solution for Dogs

- **Longest-lasting protection available in a topical solution[1]**
  - — Systemic 'nose-to-toes' protection
- **Trusted safety[1]**
  - — No treatment-related adverse events in puppies 8 to 9 weeks of age tested at 5x the maximum label dose (56 mg/kg) or known contraindications
- **Rapid onset of action and persistent efficacy – one dose can drive a flea infestation to extinction[2]**
  - — **Persistent:** In a US field study, 1 dose of BRAVECTO reduced fleas by ≥99.8% for 12 weeks[1]
- **Lasting tick protection[1]**
  - — Black-legged tick, American dog tick, and brown dog tick: ≥93.3% effectiveness 48 hours post-infestation for 12 weeks
  - — Lone star tick: ≥90% effectiveness 72 hours post-infestation for 8 weeks
- **Simplified dosing[1]**
  - — Easy-to-dose Twist'n'Use™ applicator

TOPICAL FOR DOGS

References:
1. Bravecto Topical Solution for Dogs [prescribing information]. Madison, NJ: Merck Animal Health; 2016. **2.** Freedom of Information Summary, NADA 141-459. Approved July 20, 2016.

IMPORTANT SAFETY INFORMATION: Bravecto has not been shown to be effective for 12-weeks' duration in puppies or kittens less than 6 months of age. **Bravecto Chew for Dogs:** The most common adverse reactions recorded in clinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. Bravecto is not effective against lone star ticks beyond 8 weeks of dosing. **Bravecto Topical for Dogs:** The most common adverse reactions recorded in clinical trials were vomiting, hair loss, diarrhea, lethargy, decreased appetite, and moist dermatitis/rash. Bravecto is not effective against lone star ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. Use caution in dogs with a history of seizures. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures. **Bravecto Topical for Cats:** The most common adverse reactions recorded in clinical trials were vomiting, itching, diarrhea, hair loss, decreased appetite, lethargy, and scabs/ulcerated lesions. Bravecto is not effective against American dog ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. The safety of Bravecto has not been established in breeding, pregnant and lactating cats. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving Bravecto, even in cats without a history of neurologic abnormalities.

Topical Solution for Cats

- **Longest-lasting protection available in a topical solution[1,2]**
  - — Systemic nose-to-toes protection
- **Trusted safety[1,2]**
  - — No treatment-related adverse events in kittens 11 to 13 weeks of age tested at 5x the maximum label dose (93 mg/kg) or known contraindications
- **Fewer potential gaps in protection help lessen poor compliance**
- **Rapid onset of action and persistent efficacy**
  - —one dose can drive a flea infestation to extinction[1,2]
  - — Persistent: In a US field study, 1 dose of BRAVECTO reduced fleas by ≥99% for 12 weeks[1]
  - — Fast: 100% of fleas killed 8 hours after treatment[1]
- **Lasting tick protection[1,2]**
  - — Black-legged tick: >94% effectiveness 48 hours post-infestation for 12 weeks
  - — American dog tick: >98% effectiveness 48 hours post-infestation for 8 weeks
- **Simplified dosing[1]**
  - — Easy-to-dose Twist'n'Use™ applicator

TOPICAL FOR CATS

References:
1. Bravecto Topical Solution for Cats [prescribing information]. Madison, NJ: Merck Animal Health; 2016.
2. Freedom of Information Summary, NADA 141-459. Approved July 20, 2016.

Contact your Merck Animal Health representative or distributor partner to learn more, or go to BravoVets.com

Available by veterinary prescription only. Please see full Prescribing Information on reverse side.

MERCK Animal Health

PENN Veterinary Supply, Inc.

Phone - 800.233.0210 www.pennvet.com

BRAVECTO®

(fluralaner topical solution) for Cats

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

Description:
Each tube is formulated to provide a minimum dose of 18.2 mg/lb (40 mg/kg) body weight. Each milliliter contains 280 mg of fluralaner.

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. Inactive ingredients: dimethylacetamide, glycofurol, diethyltoluamide, acetone

Indications:
Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of *Ixodes scapularis* (black-legged tick) infestations for 12 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

Bravecto is also indicated for the treatment and control of *Dermacentor variabilis* (American dog tick) infestations for 8 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds 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 18.2 mg/lb (40 mg/kg) body weight.

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

Dosage Schedule:

Body Weight Ranges (lb)	Fluralaner content (mg/tube)	Tubes Administered
2.6 – 6.2	112.5	One
>6.2 – 13.8	250	One
>13.8 – 27.5*	500	One

* Cats over 27.5 lb should be administered the appropriate combination of tubes.

Step 1: Immediately before use, open the pouch and remove the tube. 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. The cap is designed to stay on the tube for dosing and should not be removed. The tube is open and ready for application when a breaking of the seal is 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 cat. If a second spot is needed to avoid run off, then apply the second spot slightly behind the first spot.

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

Do not contact or allow children to contact the application site until dry.

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. Avoid contact with skin and eyes. If contact with eyes occurs, then flush eyes slowly and gently with water. **Wash hands and contacted skin thoroughly with soap and water immediately after use of the product.**

The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

Precautions:
For topical use only. Avoid oral ingestion. (see **Animal Safety**).

Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving Bravecto, even in cats without a history of neurologic abnormalities (see **Adverse Reactions**).

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

The safety of Bravecto has not been established in breeding, pregnant and lactating cats.

Adverse Reactions:
In a well-controlled U.S. field study, which included a total of 161 households and 311 treated cats (224 with fluralaner and 87 with a topical active control), there were no serious adverse reactions.

Percentage of Cats with Adverse Reactions (AR) in the Field Study

Adverse Reaction (AR)	Bravecto 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 ataxia and right head tilt, 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 during the study. 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 during the study.

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, there were three reports of facial dermatitis in humans after close contact with the application site which occurred within 4 days of application.

For technical assistance or to report a suspected adverse drug reaction, 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/AnimalVeterinary/SafetyHealth.

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.

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:
In a well-controlled European laboratory study, Bravecto killed 100% of fleas 8 hours after treatment and reduced the number of live fleas on cats by > 98% within 12 hours after treatment or post-infestation for 12 weeks. In well-controlled laboratory studies, Bravecto demonstrated > 94% effectiveness against *Ixodes scapularis* 48 hours post- infestation for 12 weeks. Bravecto demonstrated > 98% effectiveness against *Dermacentor variabilis* 48 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% 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 (8 cats per group). The cats 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 77°F (25°C). Store in the original package in order to protect from moisture. The pouch should only be opened immediately prior to use.

How Supplied:
Bravecto is available in three strengths for use in cats (112.5, 250, and 500 mg fluralaner per tube). Each tube is packaged individually in a pouch. Product may be supplied in 1 or 2 tubes per carton.

NADA 141-459, Approved by FDA
Distributed by:
Intervet Inc (d/b/a Merck Animal Health), Madison, NJ 07940

Made in the USA.

159363 R3 017392

Rev. 09/16

MERCK Animal Health

BRAVECTO® (FLURALANER)

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.

Precautions:
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.

For technical assistance or to report a suspected adverse drug reaction, 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/AnimalVeterinary/SafetyHealth.

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 (0X) 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, inappetant, 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 (0X) 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 treated dog suffered a seizure during the course of the study (46 days after the second 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).

How Supplied:
Bravecto 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.

NADA 141-426, Approved by FDA

Distributed by:
Intervet Inc (d/b/a Merck Animal Health)
Madison, NJ 07940

Made in Austria

154545 R1

MERCK Animal Health

BRAVECTO®

(fluralaner topical solution) for Dogs

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

Description:
Each tube is formulated to provide a minimum dose of 11.4 mg/lb (25 mg/kg) body weight. Each milliliter contains 280 mg of fluralaner.

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. Inactive ingredients: dimethylacetamide, glycofurol, diethyltoluamide, acetone

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 topically 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**).

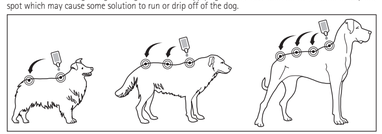
Dosage Schedule

Body Weight Ranges (lb)	Fluralaner content (mg)/tube	Tubes 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 tubes

Step 1: Immediately before use, open the pouch and remove the tube. 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. The cap is designed to stay on the tube for dosing and should not be removed. The tube is open and ready for application when a breaking of the seal is felt.

Step 2: The dog 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 between the shoulder blades of the dog.
Step 3: Squeeze the tube and gently apply Bravecto in one or more spots starting between the shoulder blades and continuing along the dog's back. Avoid applying an excessive amount of solution in any one spot which may cause some solution to run or drip off of the dog.



Bathing or water immersion 3 days after administration will not reduce the effectiveness of Bravecto against fleas and *Ixodes ricinus* ticks (see **Effectiveness**).
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
Human Warnings:
Not for human use. Keep this and all drugs out of the reach of children.

Do not contact or allow children to contact the application site until dry.

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. Avoid contact with skin and eyes. If contact with eyes occurs, then flush eyes slowly and gently with water. **Wash hands and contacted skin thoroughly with soap and water immediately after use of the product.**

The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

Precautions:
For topical use only. Avoid oral ingestion. (see **Animal Safety**).

Use with caution in dogs with a history of seizures. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures (see **Adverse Reactions** and **Animal Safety**).

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 a total of 165 households and 321 treated dogs (221 with fluralaner and 100 with a topical active control), there were no serious adverse reactions.

Percentage of Dogs with Adverse Reactions in the Field Study

Adverse Reaction (AR)	Bravecto Group: Percent of Dogs with the AR During the 105-Day Study (n= 221 dogs)	Active Control Group: Percent of Dogs with the AR During the 84-Day Study (n= 100 dogs)
Vomiting	6.3 %	6.0 %
Alopecia	4.1 %	2.0 %
Diarrhea	2.7 %	11.0 %
Lethargy	2.7 %	2.0 %
Decreased Appetite	1.4 %	0.0 %
Moist Dermatitis/Rash	0.9 %	0.0 %

In the field study, two dogs treated with Bravecto with no prior history of seizures each experienced a seizure. One dog had two seizures a day apart about 18 days after its first dose. The dog was started on antiepileptic medication and had no additional seizures during the study. A second dog had a seizure 76 days after its first dose and 3 days after starting fluoxetine for separation anxiety. The fluoxetine was discontinued and the dog experienced no additional seizures during the study. One dog treated with Bravecto was observed by the owner to be off balance for about 30 minutes five days after its first dose and had no similar observations after the second dose. One dog with a history of seizures had a seizure the day after the second dose of the active control.
In two well-controlled laboratory dose confirmation studies, one dog developed mild to moderate redness, flaking, crusts/scabs and alopecia at the treatment site from Day 1 through 14 after application of Bravecto on Day 0, and one dog developed self-limiting generalized erythema (possible allergic reaction) one day after treatment with Bravecto.
In a European field study in cats, there were three reports of facial dermatitis in humans after close contact with the application site which occurred within 4 days of application.
For technical assistance or to report a suspected adverse drug reaction, 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 wwwbravecto.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/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology:
Peak fluralaner concentrations are achieved between 7 and 42 days following topical administration and the elimination half-life ranges between 14 and 29 days. The bioavailability of fluralaner following oral and topical administration is approximately 25%.

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:
In well-controlled laboratory studies, Bravecto killed fleas and reduced the numbers of live fleas on dogs by >99% and 100% within 24 and 48 hours, respectively, post-infestation for 12 weeks. In well-controlled laboratory studies, Bravecto demonstrated ≥93.3% effectiveness against *Dermacentor variabilis*, *Ixodes scapularis* and *Rhipicephalus sanguineus* 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 ≥99.8% 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.
In a European laboratory study, Bravecto demonstrated ≥98.2% effectiveness against fleas and *Ixodes ricinus* ticks after multiple water immersion or shampooing occasions, the first occurring 3 days after application, for 12 weeks.

Animal Safety:
Margin of Safety Study: In a margin of safety study, Bravecto was administered topically to 8- to 9-week-old-puppies at 1, 3, and 5X the maximum labeled dose of 56 mg/kg at three, 8-week intervals (8 dogs per group). The dogs in the control group (0X) were administered 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. Five of the six treated dogs experienced salivation immediately after administration. One treated animal experienced loose feces with blood three hours after administration. One treated animal experienced vomiting eight hours after administration.
Oral Safety Study: In a safety study, one dose of Bravecto topical solution was administered orally to 8- to 10-month-old-puppies at 1X the maximum labeled dose of 56 mg/kg. The dogs 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. Five of the six treated dogs experienced salivation immediately after administration. One treated animal experienced loose feces with blood three hours after administration. One treated animal experienced vomiting eight hours after administration.
Reproductive Safety: Reproductive safety was evaluated with the oral tablet formulation of fluralaner (see **Clinical Pharmacology**). Bravecto tablets were administered to intact, reproductively- sound male and female Beagles at a dose of up to 168 mg/kg (equivalent to 3X the maximum treatment dose) on three to four occasions at 8-week intervals. The dogs in the control group (0X) 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 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, steroids and sedatives.

Storage Information:
Do not store above 77°F (25°C). Store in the original package in order to protect from moisture. The pouch should only be opened immediately prior to use.

How Supplied:
Bravecto is available in five strengths for use in dogs (112.5, 250, 500, 1000, and 1400 mg fluralaner per tube). Each tube is packaged individually in a pouch. Product may be supplied in 1 or 2 tubes per carton.

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