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

Effectiveness (see Adverse Reactions)

Bravecto is effective against *A. americanum* and *D. variabilis* (see Adverse Reactions), which are the predominant tick species in the United States. Bravecto demonstrated > 90% effectiveness beyond 8 weeks against *D. variabilis* and > 94% effectiveness against *I. scapularis* (black-legged tick) infestations for 8 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 6 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:**

<table>
<thead>
<tr>
<th>Body Weight Ranges (lb)</th>
<th>Fluralaner content (mg/tube)</th>
<th>Tubes Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6 – 6.2</td>
<td>112.5</td>
<td>One</td>
</tr>
<tr>
<td>&gt;6.2 – 13.8</td>
<td>250</td>
<td>One</td>
</tr>
<tr>
<td>&gt;13.8 – 22.57</td>
<td>500</td>
<td>One</td>
</tr>
</tbody>
</table>

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

**Step 1:** Immediately before, open the pouch and remove the tube. Hold the tube at the crimped end with the cap at 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.

**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 *D. variabilis* 48 hours post-infestation for 12 weeks. Bravecto demonstrated > 98% effectiveness against *D. 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. All treated kittens experienced salivation and four of six experienced coughing immediately after administration. One treated kitten experienced vomiting 2 hours after administration.

**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.

**Indications:**

Bravecto is indicated for the treatment and control of *Dermacentor variabilis* ticks beyond 8 weeks after dosing (see Effectiveness).

In the field study, two cats treated with fluralaner topical solution experienced ataxia. One cat became atactic 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, recurred 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 atactic 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.

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

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

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percent of Cats with the AR During the 105-Day Study</th>
<th>Control Group: Percent of Cats with the AR During the 8-Day Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7.6%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>5.4%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Alopecia</td>
<td>4.9%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>3.6%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>3.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Scabs/Ulcereated Lesions</td>
<td>2.2%</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

During the 105-Day Study, all treatments were well tolerated. The most commonly reported adverse reactions were vomiting, diarrhea, decreased appetite, and lethargy. The frequency of vomiting was similar between the Bravecto and control groups. Diarrhea was more common in the control group than in the Bravecto group. Decreased appetite and lethargy were more common in the Bravecto group than in the control group. Scabs and ulcereated lesions were rare and similar in incidence between the Bravecto and control groups.

In a safety study, one dose of Bravecto topical solution was administered orally to six cats 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. 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 vaccinations, anthelmintics, antibiotics, steroids and sedatives. No adverse reactions were observed from the concurrent use of Bravecto with other medications.

**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).

This product has not been evaluated for efficacy against *A. americanum* in cats weighing less than 5.5 pounds.