Bravecto® 1-Month (fluralaner) Chews for Dogs

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

Description:
Bravecto 1-Month (fluralaner) is a flavored chew formulated to provide a minimum dose of 4.5 mg/lb (10 mg/kg) body weight of fluralaner. The chemical name of fluralaner is (S)-4-[5-(2,5-dichlorophenyl)-5-(trifluoromethyl)-2-methyl-N-[2-oxo-2-(2,2,2-trifluoroethyl)aminomethyl]benzamid]-[2-oxo-2-(2,2,2-trifluoroethyl)aminomethyl]benzamid.

Dosage Schedule:

<table>
<thead>
<tr>
<th>Body Weight Range (lb)</th>
<th>Fluralaner content (mg)</th>
<th>Chews Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4 - 9.9</td>
<td>45</td>
<td>One</td>
</tr>
<tr>
<td>&gt;9.9 - 22.0</td>
<td>100</td>
<td>One</td>
</tr>
<tr>
<td>&gt;22.0 - 44.0</td>
<td>200</td>
<td>One</td>
</tr>
<tr>
<td>&gt;44.0 - 88.0</td>
<td>400</td>
<td>One</td>
</tr>
<tr>
<td>&gt;88.0 - 123.0</td>
<td>560</td>
<td>One</td>
</tr>
</tbody>
</table>

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

Adverse Reactions:

In a well-controlled U.S. field study, which included 271 dogs (201 dogs were administered Bravecto 1-Month every 30 days and 70 dogs were administered an oral active control [an isoxazoline] every 30 days), there were no serious adverse reactions associated with treatment. Over the 90-day study period, all observations of potential adverse reactions were recorded.

Bravecto 1-Month is not effective against *A. americanum* in puppies less than 6 months of age (see Effectiveness).

The safety of Bravecto 1-Month has not been evaluated in breeding, pregnant and lactating dogs (see Animal Safety).

Role of Adverse Reactions in the Field Study:

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Fluralaner Group: Percentage of Dogs with the AR during the 90-Day Study (n=201 dogs)</th>
<th>Active Control Group: Percentage of Dogs with the AR during the 90-Day Study (n=70 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>7.0%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.0%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3.0%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>3.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Liver enzymes (serum ALT or ALP) greater than twice the upper reference range*</td>
<td>1.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>1.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Weight loss (&gt;15%)</td>
<td>0.5%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

One dog in the Bravecto 1-Month group with a history of seizures managed with anticonvulsant medication had seizure activity 28 days after its first dose; the dog received its second dose later the same day. No additional seizures occurred during the study. One dog in the control group with no history of seizures had seizure activity 12 days after its second dose. The dog was started on anticonvulsant medication and no additional seizures occurred during the study.

During the palatability assessment, four dogs coughed within 1 hour of dosing with Bravecto 1-Month. Palatability was not assessed in the control group.

In well-controlled laboratory effectiveness studies, one dog and three puppies administered Bravecto 1-Month had diarrhea (with or without blood).

*Some common observations occurring at a similar incidence in the treated and control groups.*

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.

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Reproductive Safety Study:
Reproductive safety was evaluated for fluralaner, the active ingredient in BRAVECTO 1-Month (fluralaner). Fluralaner was administered orally to intact, reproductively-sound male and female Beagles at a dose of up to 168 mg/kg on three to four occasions at 8-week intervals. The dogs in the control group 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 dog in the treated group 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 1-Month was used concurrently with other medications, such as vaccines, anthelmintics, antibiotics (including topicals), steroids, analgesics, and anesthetics. No adverse reactions were observed from the concurrent use of Bravecto 1-Month with other medications.

Storage Conditions:
Do not store above 86°F (30°C).

How Supplied:
Bravecto 1-Month is available in five strengths (45, 100, 200, 400, and 560 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, 3, or 4 chews per package.

Approved by FDA under NADA # 141-532
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Rev: 08/2021