The available once-a-month prescription tablet that prevents heartworm disease and fleas populations in dogs and puppies, SENTINEL® FLAVOR TABS® (milbemycin oxime/lufenuron) also control flea populations and adult hookworms, and remove and control adult roundworms and whirlemos infections in dogs and puppies.

**Caution**

Dr. Frits V. Flytzanis, VMD, USA law restricts this drug to use by or on the order of a licensed veterinarian.

**Warnings**

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

**Description**

SENTINEL® FLAVOR TABS are available in four tablet sizes in color-coded packages for administration to dogs and puppies according to their weight. (See Dosage section.) Each tablet is formulated to provide a minimum of 0.25 mg/kg (0.5 mg/kg) of milbemycin oxime and 1.65 mg/kg (3 mg/kg) body weight of lufenuron.

Milbemycin oxime consists of the oxime derivative of 5-didehydrothiabenzimidazolines in the ratio of approximately 80% A (C19H18NO3, MW 557.7) and 20% A (C19H16NO2, MW 541.8). Milbemycin oxime is classified as a macrocyclic lactone.

Lufenuron is a benzenoxyliurane derivative with the following chemical composition: \(\text{C}_{12} \text{H}_{11} \text{N}_{2} \text{O}_{5}\). Lufenuron is classified as a systemic insecticide and acaricide (as a neonicotinoid). Lufenuron can be used to control fleas, lice, and ticks in dogs and puppies.

**Mode of Action**

Milbemycin oxime, one active ingredient in each tablet of SENTINEL® FLAVOR TABS, is a macrocyclic antibiotic which is believed to act by interfering with invertebrate neurotransmission. Milbemycin oxime eliminates the fast action of Ach on the motor nerve and the slow action of Ach on the slow nerve. The slow action of Ach is believed to be the slow neurovascular response (VN) of the heart. Lufenuron is an insect development inhibitor which breaks the flea life cycle by inhibiting egg development. Lufenuron’s mode of action is interference with chitin synthesis, polymerization and deposition. Lufenuron has no effect on the adults, but by killing the larval stages of the flea, it disrupts the cycle and hence prevents the development of new adult fleas. Lufenuron, therefore, is a systemic insecticide and acaricide (as a neonicotinoid). Lufenuron can be used to control fleas, lice, and ticks in dogs and puppies.

**Precautions**

Do not use in puppies less than four weeks of age and in dogs less than five pounds in weight. Prior to administration of SENTINEL® FLAVOR TABS, dogs should be tested for existing roundworm populations. Infected dogs should be treated to remove adult heartworms and microfilariae prior to initiating treatment with SENTINEL® FLAVOR TABS. Treatment of heartworm infected dogs with any antihelminthic should only be done after consultation with your veterinarian. Lufenuron, metronidazole, and other anthelmintics have been shown to cause seizures, vomiting, salivation and lethargy in some cases. Do not use the drug if the dog is allergic to any of the ingredients.

**Efficacy**

Milbemycin Oxime

In laboratory studies, the single dose of milbemycin oxime at 0.5 mg/kg was effective in removing roundworms, hookworms and whipworms. In well-controlled clinical field studies, 768 dogs completed treatment with milbemycin oxime. Milbemycin oxime was also effective in removing roundworms and whipworms and in controlling hookworms.

Lufenuron

Lufenuron provided 98% control of flea egg development for 32 dogs following a single dose of lufenuron at 10 mg/kg in studies using experimental flea infestations. In well-controlled clinical trials, when treatment with lufenuron tablets was initiated prior to the flea season, mean flea counts were lower on lufenuron-treated dogs versus placebo-treated dogs (by 70% to 80%) compared with dogs not treated with lufenuron. The mean number of fleas on lufenuron-treated dogs was approximately 4 compared to 200 on placebo-treated dogs.

**Safety**

Milbemycin Oxime

Milbemycin oxime has been tested safely in over 75 different breeds of dogs, including collies, pregnant females, breeding males and females, and puppies over two weeks of age. In well-controlled clinical field studies, 768 dogs completed treatment with milbemycin oxime. Milbemycin oxime was used safely in animals receiving frequently used veterinary products such as vaccines, antibiotics, steroids, flea, ticks, and heartworm medication.

Two studies in heartworm-infected dogs were conducted which demonstrated milbemycin oxime had no effect on the weights of dogs. Treatment with SENTINEL® FLAVOR TABS reduced the risk of heartworm disease in dogs.

Lufenuron

Lufenuron tablets have been used and tested safely in over 20 breeds of dogs, including pregnant females, breeding males and puppies over six weeks of age. In well-controlled clinical trials, 100 dogs completed treatment with lufenuron tablets. Lufenuron tablets were used safely in animals receiving frequently used veterinary products such as vaccines, antibiotics, anesthetics and steroids. In a 6-month study, doses up to 10x recommended dose of 10 mg/kg body weight had no effect on body weight.

A rising-dose safety study conducted in rough-coated coiffes manifested a clinical reaction consisting of alopecia, pyrexia and periodic recurvency in one of 10 dogs treated with milbemycin oxime at 12.5 mg/kg (50x monthly dose rate). Prior to receiving the 12.5 mg/kg body weight dose of milbemycin oxime on day 57 of the study, all animals had undergone an escalating dosing regimen consisting of 2.5 mg/kg milbemycin oxime (5X monthly use rate) on day 0, followed by 5.0 mg/kg (10X monthly use rate) on day 20 and 10.0 mg/kg (10X monthly use rate) on day 32. No adverse reactions were observed in any of the coiffes treated with the escalating dose regimen up through the 57th day of study.

Safety: Lufenuron

Lufenuron tablets have been used and tested safely in over 20 breeds of dogs, including pregnant females, breeding males and puppies over six weeks of age. In well-controlled clinical trials, 100 dogs completed treatment with lufenuron tablets. Lufenuron tablets were used safely in animals receiving frequently used veterinary products such as vaccines, antibiotics, anesthetics and steroids. In a 6-month study, doses up to 10x recommended dose of 10 mg/kg body weight had no effect on body weight.

A single dose of 200 mg/kg (100X the recommended dose rate) had no marked effect on adult dogs, but caused decreased activity and appetite in eight weeks old puppies. Mean body weights of male and female puppies were lower in treated versus control group at the end of the study. In specifically designed large animal safety studies, lufenuron tablets were tested with concurrent administration of flea adulticides containing carboxylic acids, pyrethroids and phosalone. No toxicity resulted from these combinations. Lufenuron tablets did not cause cholinesterase inhibition nor did they enhance cholinesterase inhibition caused by exposure to organophosphates.

Four reproductive safety studies were conducted in breeding dogs with lufenuron tablets: two laboratory and two well-controlled clinical studies. In one of the laboratory studies, where lufenuron was administered to beagle dogs at doses equivalent to 90X (2X daily) the recommended dose of milbemycin oxime (5X monthly use rate), the ratio of gravid females to females mated was 8/8 or 100% in the group control and 8/8 or 100% in the lufenuron-treated group. The mean number of pups per litter was two animals higher in the treated versus control groups and the mean body weights of pups from treated animals in this study was lower than from control groups.

These pups grew at a similar rate to control pups. There was a higher incidence of four clinical signs in the lufenuron-treated versus control groups; nasal discharge, pulmonary congestion, diaphragmatic reflux and increased body weight. This was transient or self-resolving. The incidence of these four clinical signs in the treated groups during the 14 days following treatment of lufenuron tablets was 6% (2X dose) or lower.

Results from three additional reproductive safety studies, laboratory and two clinical studies evaluating eleven breeds of dogs. did not demonstrate any adverse findings for the reproductive parameters measured including fertility, pup birth weights and pup clinical signs. Administration of lufenuron up to 5X the recommended daily dose to beagle dogs did not cause adverse effects.

Data from analyses of milk of lactating animals treated with lufenuron tablets at 2X and 6X the recommended monthly use rate demonstrated that lufenuron concentrates in the milk of these dogs. The average milk concentration ratio was 60X (6X higher drug concentrations in milk compared to drug levels in blood of treated females). Nursing puppies averaged 8-9 times higher blood concentrations of lufenuron compared to their dams.

**Dosage**

SENTINEL® FLAVOR TABS are given orally, once a month. At the recommended minimum dose of 0.23 mg/kg milbemycin oxime and 4.55 mg/kg lufenuron per tablet. Dogs over 100 lbs are provided the appropriate combination of tablets.

**Administration**

TO ENSURE ADEQUATE ABSORPTION

ALWAYS ADMINISTER SENTINEL FLAVOR TABS TO DOGS IMMEDIATELY AFTER OR IN CONJUNCTION WITH A NORMAL MEAL.

**SENTINEL FLAVOR TABS**

**Recommended Dosage Schedule**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Milbemycin Oxime</th>
<th>Lufenuron</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 to 10 lbs.</td>
<td>2.3 mg</td>
<td>96 mg</td>
</tr>
<tr>
<td>11 to 25 lbs.</td>
<td>5.75 mg</td>
<td>175 mg</td>
</tr>
<tr>
<td>26 to 50 lbs.</td>
<td>11.5 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>51 to 100 lbs</td>
<td>23 mg</td>
<td>460 mg</td>
</tr>
</tbody>
</table>

**How Supplied**

SENTINEL® FLAVOR TABS are available in four tablet sizes (see Dosage section) formulated according to the weight of the dog. Each tablet size is available in color-coded packages of 8 or 12 tablets each, which are packaged 10 per display carton.

**Storage Conditions**

Store in a dry place at controlled room temperature between 59° and 77°F (15°-25°C).