Chewable Tablets

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

Description: TRIFEXIS is a macrocyclic lactone anthelmintic, containing two major factors, A3 and A4 of the chemical compositions C41H65NO10 and C42H67NO10, respectively. Milbemycin oxide is a macrocyclic lactone antibiotic, containing two main factors, A3 and A4 of milbemycin oxide. The approximate ratio of A4/A3 is 20:60. Milbemycin A4-5-oxime has the chemical composition of C42H67NO10. Milbemycin oxide is a macrocyclic lactone antibiotic, containing two main factors, A3 and A4 of milbemycin oxide. The approximate ratio of A4/A3 is 20:60. Milbemycin A4-5-oxime has the chemical composition of C42H67NO10.

Dosage Schedule:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Spinosad Per Tablet (mg)</th>
<th>Milbemycin Per Tablet (mg)</th>
<th>Tablets Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10 lbs</td>
<td>140</td>
<td>2.3</td>
<td>One</td>
</tr>
<tr>
<td>10.1-20 lbs</td>
<td>270</td>
<td>4.5</td>
<td>One</td>
</tr>
<tr>
<td>20.1-40 lbs</td>
<td>560</td>
<td>9.3</td>
<td>One</td>
</tr>
<tr>
<td>41-60 lbs</td>
<td>870</td>
<td>13.5</td>
<td>Two</td>
</tr>
<tr>
<td>61-120 lbs</td>
<td>1620</td>
<td>27</td>
<td>One</td>
</tr>
</tbody>
</table>

Over 120 lbs Administer the appropriate combination of tablets.

Adverse Reactions:

TRIFEXIS should be administered at monthly intervals beginning within 1 month of the dog’s first seasonal exposure and continuing until at least 1 month after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS). TRIFEXIS may be administered year round without interruption. When replacing another heartworm preventative product, TRIFEXIS should be given within a month of the last dose of the former medication.

Flea and Treatment Prevention:

TREATMENT WITH TRIFEXIS IS NOT INDICATED FOR MICROFILARIA CLEARANCE. While the number of circulating microfilariae may decrease following treatment, TRIFEXIS is not indicated for microfilariae clearance. Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with spinosad alone, a component of TRIFEXIS (see ADVERSE REACTIONS). TRIFEXIS and the associated adverse reactions are listed in decreasing order of frequency:

- Vomiting
- Pruritus
- Lethargy
- Diarrhea
- Dermatitis
- Skin reddening
- Nausea
- Pinnal reddening

Adverse Reactions:

TRIFEXIS is indicated for the prevention of heartworm disease (Dirofilaria immitis). TRIFEXIS kills fleas and is indicated for the prevention and treatment of flea infestations (Ctenocephalides felis) and the treatment and control of adult hookworm (Ancylostoma caninum, adult roundworm (Toxocara canis) and Toxocara jevisi) and adult whipworm (Trichuris vulpis) infections in dogs and puppies 6 weeks of age or older and 5 pounds of body weight or greater.

Dosage and Administration:

TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxide body weight. For heartworm prevention, give once monthly for at least 3 months after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS). TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxide body weight. For heartworm prevention, give once monthly for at least 3 months after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS). TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxide body weight. For heartworm prevention, give once monthly for at least 3 months after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS).

Heartworm Prevention:

TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxide body weight. For heartworm prevention, give once monthly for at least 3 months after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS).

Adverse Reactions:

TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxide body weight. For heartworm prevention, give once monthly for at least 3 months after the dog’s last seasonal exposure to mosquitoes (see EFFECTIVENESS). This finding is unknown.

Post Approval Experience (Mar 2012):

The following adverse reactions are based on post approval adverse drug reaction reporting. The adverse reactions are listed in decreasing order of frequency:

- Puppies less than 14 weeks of age may experience a higher rate of vomiting due to treatment-related adverse reactions.

Adverse Reactions:

TRIFEXIS is available in five tablet sizes. Each tablet size is available in color-coded packages of 6 tablets.

- 5-10 lbs (140 mg spinosad and 2.3 mg milbemycin)
- 10.1-20 lbs (270 mg spinosad and 4.5 mg milbemycin)
- 20.1-40 lbs (560 mg spinosad and 9.3 mg milbemycin)
- 41-60 lbs (870 mg spinosad and 13.5 mg milbemycin)
- 61-120 lbs (1620 mg spinosad and 27 mg milbemycin)

NADA 141-321, Approved by the FDA

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In a margin of safety study, TRIFEXIS was administered orally to 6-week-old Beagle puppies at doses of 1, 3, and 5 times the upper half of the therapeutic dose band, every 28 days for 6 dosing periods. Vomiting was seen in all groups during the course of the study. Adverse reactions seen during the course of the study were salivation, decreased activity, coughing and salivating.

Body weights were similar between control and treated groups throughout the study. Treatment with TRIFEXIS was not associated with any clinically significant hematology, clinical chemistry or gross necropsy changes. One Beagle had minimal glomerular fibrosis observed microscopically. The clinical relevance of this finding is unknown.

In an avermectin-sensitive Collie dog study, TRIFEXIS was administered orally at 1, 3, and 5 times the upper half of the therapeutic dose band to Beagle dogs with adult heartworm infections and circulating microfilariae, every 28 days for 3 treatment cycles. Vomiting was seen in one dog in the 1X group, in three dogs in the 3X group, and in one dog in the 5X group. But all one incident of vomiting was seen in one dog during the 6-month period. Vomiting was mild and self-limited. Hypermobility reactions were not observed in any of the treatment groups. Microfilaria counts decreased with treatment.

In a margin of safety study, 1X and 3X dosing were administered to 6-week-old Beagle puppies. Adverse reactions observed in the treatment groups with TRIFEXIS were vomiting and dizziness. Body weights in all treatment groups were comparable to the control group, with mild and self-limited symptoms. Heartworm populations in the treatment groups were comparable to the control group during treatment and post-parasiticide phases of the study. Gestations in the control group were generally smaller and less coordinated than its littermates and had fewer pups. The relationship between spinosad and milbemycin oxide treatment and the unthrifty 1X group pup are unknown. The incidence of cleft palate is not unexpected based on the historical data collected at the breeding site. In a safety margin study with spinosad alone, 6-week-old female Beagle puppies were administered average doses of 1.5, 4.4, and 7.4 times the maximum dosages received during the 6-month period. Vomiting was observed across all treatments, including controls, and was observed at an increased rate at elevated doses. Vomiting most often occurred 1 hour after dosing, occurred more frequently, and increased in severity as day weight was reduced. Puppies were dead or moribund at 24 weeks of age.

Storage Information:

Store below 60°F (16-77°F), excursions permitted between 15-30°C (59-86°F).

How Supplied:

TRIFEXIS is available in five tablet sizes. Each tablet size is available in color-coded packages of 6 tablets.

Usage:

In the US field study, TRIFEXIS was administered orally at 1, 3, and 5 times the upper half of the therapeutic dose band to Beagle dogs with adult heartworm infections and circulating microfilariae, every 28 days for 3 treatment cycles. Vomiting was seen in one dog in the 1X group, in three dogs in the 3X group, and in one dog in the 5X group. But all one incident of vomiting was seen in one dog during the 6-month period. Vomiting was mild and self-limited. Hypermobility reactions were not observed in any of the treatment groups. Microfilaria counts decreased with treatment.