Technical Profile

EFFITIX™ Topical Solution for Dogs and EFFIPRO® Topical Solution for Cats: Fipronil-Based Options from Virbac
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EFFITIX™ Topical Solution for Dogs

EFFITIX Topical Solution for Dogs is a fipronil and permethrin combination product from Virbac Animal Health for use in dogs older than 12 weeks of age. EFFITIX Topical Solution for Dogs is unique in that it contains 2 insecticides, fipronil and permethrin, which results in a rapid speed of kill for fleas as well as long-lasting acaricidal efficacy and repellency due to the action of permethrin. Following application, EFFITIX Topical Solution for Dogs has residual parasite-killing properties over the monthly treatment interval.

Fipronil: The Antiparasitic Molecule of Reference

Fipronil was discovered and developed by Rhône-Poulenc in the 1980s and has been available for more than 2 decades in veterinary medicine as a topical ectoparasiticide.

Fipronil is a well-known insecticide and acaricide of the phenylpyrazole family, effective against fleas, ticks, mites, and lice. It has low solubility in water, but is very soluble in fatty substances and is stable at room temperature. Following application to the skin, fipronil dissolves in the skin’s oily sebaceous layer and spreads across the skin surface. It is concentrated in the sebaceous gland, the epithelial layers surrounding the hairs, and the exposed part of the hair shaft after treatment.

The chemical name for fipronil is (±)-5-amino-1(2,6-dichloro-α,α,α-trifluoro-ρ-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile.
Fipronil is a potent compound that disrupts the insect central nervous system (CNS) by acting on gamma-aminobutyric acid type A (GABA-A)–regulated chloride channels. GABA is a chemical messenger that is widely distributed in the CNS. The normal binding of GABA to the receptors on the chloride channels blocks the transmission of the nerve impulse, preventing excessive stimulation of the parasite’s CNS. Because of this property, GABA is classified as an inhibitory neurotransmitter, as opposed to excitatory neurotransmitters, such as glutamate, that increase nerve impulses in neurons. Fipronil acts as a noncompetitive antagonist on GABA-A gated chloride channels. When the GABA-A receptor system is blocked by fipronil, the net result is neuronal hyperexcitation. This causes excitation and convulsions in insects and acarids and death by disruption of the nervous system.

Fipronil is toxic to insects and acarids by contact. It enters the parasite either by being absorbed through the cuticle following contact or by ingestion.
Fipronil is a **broad-spectrum insecticide and acaricide** used to control cockroaches, ants, fleas, mole crickets, ticks, mites, subterranean termites, and agricultural pests. On dogs, fipronil has an excellent insecticidal and acaricidal activity against fleas (*Ctenocephalides felis*), ticks (*Rhipicephalus sanguineus*, *Ixodes scapularis* and *I. pacificus*, *Dermacentor variabilis* and *D. andersoni*, *Amblyomma americanum* and *A. maculatum*), and lice (*Trichodectes canis* and *Felicola subrostratus*). Fleas and ticks are killed within 24 hours and 48 hours of contact with fipronil, respectively.

Fipronil exhibits differential binding affinity for GABA receptor subunits, with a much higher binding affinity for insect/acarine receptor complexes than for mammalian receptor complexes. Thus, the compound has a wide margin of safety in dogs and cats. Fipronil is highly toxic to aquatic invertebrates (crustaceans, zooplankton), bees, termites, rabbits, pheasants, partridges, quail, and many fish (varying by species). It is relatively innocuous to songbirds, waterfowl, and earthworms. In dogs, slight skin irritation can result from direct, short-term contact. Excessive salivation, vomiting, tremors, incoordination, and seizures have been reported after ingestion. In humans, sweating, nausea, vomiting, headaches, stomach pain, dizziness, weakness, and seizures have been reported. The clinical signs observed following a brief exposure generally improve without treatment.

**Permethrin: Acaricidal Impact With the Benefit of Repellency**

**Permethrin** is part of the pyrethroid class (type I) of pesticides and was first registered in 1979. Pyrethroids are organic chemicals derived from natural pyrethrins produced by chrysanthemums. Small changes to the pyrethrum molecule have increased activity against parasites while increasing the stability and decreasing mammalian toxicity.

A broad-spectrum, non-systemic insecticide, it has been used on crops, livestock and their housing, buildings, mosquito abatement programs, and to treat clothing and head lice.

Pyrethroids are fast-acting insecticides/acaricides and are degraded very slowly in ultraviolet light. They are “sticky” molecules and adhere readily to natural and synthetic fibers, including animal hair.
The chemical name for permethrin is 3-phenoxybenzyl (1RS)-cis-trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate.

**Permethrin**, as well as other pyrethroids, acts by disrupting the normal nerve function of the parasite, preventing the voltage-gated sodium channels from closing normally. During a nerve impulse, the channels on the neuron typically open, causing stimulation, then close to terminate the nerve signal. Permethrin binds to this gate protein, prolonging the excitation of the neuron, causing it to repetitively fire. Parasites lose control of their nervous system, are unable to produce coordinated movement, and die. This explains the tremors exhibited by the parasites.

**Permethrin is a fast-acting adulticide and repellant of fleas, ticks, mosquitoes, biting flies, mites, and lice.** It has rapid knockdown and repellency. This rapid killing in addition to prevention of attachment can be important when considering the pathogenesis of vector-borne diseases in dogs.

Following application, the lipophilic topical pyrethroids spread across the skin surface of the dog, dissolved in the sebaceous layer of the skin. The pyrethroids bind tightly to the hair shaft when they reach the hair follicle and persist there.

Permethrin requires the contact of the insect or tick with the chemical compound to repel them, after which it is absorbed through the cuticle of the parasite. The compound exerts a toxic effect on the nerves of the parasite, acting as a noxious stimulus, causing a flushing effect where the fleas become hyperactive. Ticks will exhibit a “hot foot” behavior, scurrying across the animal, eventually falling off and dying, before feeding can occur. Mosquitoes and biting flies require contact before being repelled.
Pyrethroids are also toxic to crustaceans, fish, and bees. They are relatively non-toxic to most mammals and birds due to rapid metabolization. Ingestion of high doses in dog feeding studies failed to cause toxicity. Vomiting and diarrhea have been reported in some dogs treated with topical formulations containing permethrin. Topical application to dog and human skin has been associated with a transient itching and/or burning sensation.

**Permethrin should not be used on cats.** Cats are not able to rapidly metabolize these compounds. After topical application, cats will ingest the product while grooming. Signs of toxicosis in cats may include tremors, drooling, lack of appetite, vomiting, diarrhea, incoordination, hyperactivity, disorientation, vocalization, depression, difficulty breathing, and seizures. **Death is possible if cats are not immediately treated appropriately.**

**Product Description and Dosing**

**KEEP OUT OF REACH OF CHILDREN**

**Indication:** EFFITIX Topical Solution for Dogs is indicated for use in DOGS (12 weeks old or older) to repel and kill fleas, ticks (brown dog tick, American dog tick, lone star tick, and deer tick), and mosquitoes; to kill biting and chewing lice and to aid in control of mites; and to repel and prevent blood feeding by biting flies.

**Hazards to Humans:** Harmful if swallowed. Causes eye irritation. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

**Hazards to Domestic Animals: For external use on dogs ONLY.** Do not use on dogs under 12 weeks of age. Individual sensitivities, while rare, may occur after using ANY pesticide product. Dogs may experience some temporary irritation at the site of product application. If signs of sensitivity occur, bathe your pet with mild soap or shampoo and rinse with large amounts of water. If signs of sensitivity occur and persist, contact a veterinarian immediately. If your dog has an unusual reaction to the initial application, consult a veterinarian before repeating application. Certain medications can interact with pesticides. Consult a veterinarian before using on medicated, debilitated, aged, pregnant, or nursing dogs, or animals known to be sensitive to pesticide products.
DO NOT USE ON CATS—If ingested BY A CAT that actively grooms a recently treated dog, this product may have serious harmful effects. If this occurs, contact your veterinarian immediately. DO NOT USE ON RABBITS.

Directions for Use: For external use on dogs ONLY. Do not use on dogs under 12 weeks of age. Do not split tubes between dogs. Do not use multiple tubes on one dog. Weigh your dog to be sure you are applying the correct dose formulated for the weight of your dog. Overdosing your dog can result in serious illness. Do not bathe your dog within the first 24 hours after the product has been applied. If your dog is exhibiting signs of and/or is being treated for skin problems, talk to your veterinarian before applying any topical flea and tick control product. Do not apply more often than once a (per) month (every 30 days).

Active Ingredients: Fipronil/permethrin. EFFITIX Topical Solution for Dogs contains 6.01% fipronil and 44.88% permethrin on a by-weight basis.

Packaging: EFFITIX Topical Solution for Dogs is packaged as plastic dispensing applicators that are available in 1-, 3-, 6-, and 36-dose packs in various sizes. Doses are determined based on age and body weight (Table 1).

Table 1. Packaging for EFFITIX Topical Solution for Dogs

<table>
<thead>
<tr>
<th>Box color</th>
<th>Dose</th>
<th>Concentrations of active ingredients (by weight)</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow</td>
<td>0.034</td>
<td>6.01% fipronil and 44.88% permethrin</td>
<td>For small dogs ≥ 12 weeks old and weighing up to 22.9 lbs</td>
</tr>
<tr>
<td>Purple</td>
<td>0.068</td>
<td>6.01% fipronil and 44.88% permethrin</td>
<td>For medium dogs weighing 23.0–44.9 lbs</td>
</tr>
<tr>
<td>Pink</td>
<td>0.135</td>
<td>6.01% fipronil and 44.88% permethrin</td>
<td>For large dogs weighing 45.0–88.9 lbs</td>
</tr>
<tr>
<td>Brown</td>
<td>0.203</td>
<td>6.01% fipronil and 44.88% permethrin</td>
<td>For extra large dogs weighing 89–132 lbs</td>
</tr>
</tbody>
</table>

Storage Conditions: Store in original container only, out of reach of children and animals.
Application Directions:

1. Remove one applicator from packaging. Hold applicator upright and remove cap. (Diagram 1)

2. Invert cap and place other end back onto applicator tip. Push cap down to break seal. Remove cap prior to treatment application. (Diagram 2)

3. Part dog’s hair until skin is visible. Place applicator tip directly against exposed skin. (Diagram 3)

3a. For small dogs (12 weeks old or older) and up to **22.9 lbs**. Deposit by squeezing the entire applicator contents onto dog’s skin, at a single site, between the shoulder blades as shown in diagram 3a.

3b. For medium dogs **23–44.9 lbs** or large dogs **45–88.9 lbs**. Apply the product evenly to three spots on the dog’s back, starting between the shoulder blades and continuing on to the second and third spots as shown in diagram 3b, squeezing the applicator until empty.

3c. For extra large dogs **89–132 lbs**. Apply the product evenly to four spots on the dog’s back, starting between the shoulder blades and continuing on to the second, third, and fourth spots as shown in diagram 3c, squeezing the applicator until empty.

Ensure that EFFITIX Topical Solution for Dogs is not applied superficially on dog’s hair.
**Frequency of Application:** Fleas, ticks, and lice (biting and chewing) infestations can be controlled with monthly applications of EFFITIX Topical Solution for Dogs. Biting flies and mosquitoes are also repelled by EFFITIX Topical Solution for Dogs.

- **Fleas:** EFFITIX Topical Solution for Dogs can start killing adult fleas within 6 hours and lasts for up to a month. Apply monthly if dog has fleas that may cause flea allergy dermatitis (FAD) or if re-infestation is likely.

- **Ticks:** EFFITIX Topical Solution for Dogs can kill ticks for up to a month. Apply monthly where tick control is consistently needed.

- **Lice:** EFFITIX Topical Solution for Dogs can kill biting and chewing lice for a month. Apply monthly where lice control is consistently needed.

- **Mites:** EFFITIX Topical Solution for Dogs aids in the control of mite infestations that may cause sarcoptic mange.

- **Biting Flies and Mosquitoes:** When applied monthly, EFFITIX Topical Solution for Dogs prevents blood feeding by and repels biting flies and mosquitoes for up to 4 weeks. Kills mosquitoes for up to 4 weeks.
## Technical Profile

### Product Features and Benefits

<table>
<thead>
<tr>
<th>Feature</th>
<th>Advantage</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Versatility in dispensing with 4 presentation sizes</td>
<td>1-dose and 36-dose packages are available in addition to the traditional 3-dose and 6-dose presentations</td>
<td>The 1-dose package provides veterinarians with an EPA-approved option for selling product on a month-to-month basis. The 1-dose package also presents an opportunity for monthly home delivery. The 36-dose package is great for sampling and for adjusting for the changing needs of young dogs &gt; 12 weeks of age as they grow through different weight ranges</td>
</tr>
<tr>
<td>Dual acaricide with repellency</td>
<td>The only veterinary product that adds permethrin to fipronil, the #1 selling active ingredient for flea and tick control</td>
<td>The addition of permethrin gives EFFITIX Topical Solution for Dogs 2 ways to work against ticks. Permethrin repels ticks, reducing the risk of disease transmission</td>
</tr>
<tr>
<td>Waterproof</td>
<td>Both fipronil and permethrin are insoluble in water. Fipronil concentrates in the hair follicles and permethrin binds to the hair shaft</td>
<td>Protection that lasts for the entire month even in dogs with exposure to water</td>
</tr>
<tr>
<td>Rapid speed of kill for fleas</td>
<td>Starts killing adult fleas within 6 hours</td>
<td>Rapidly kills fleas that may cause flea allergy dermatitis</td>
</tr>
<tr>
<td>International experience</td>
<td>Over 3 years of international experience selling fipronil-based products</td>
<td>You can buy from a company with experience manufacturing and supporting fipronil-based products</td>
</tr>
<tr>
<td>A company you can trust</td>
<td>Virbac Animal Health is the largest company in the world that is dedicated only to the animal health industry</td>
<td>Veterinarians can buy from a company that partners with veterinarians</td>
</tr>
</tbody>
</table>
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Efficacy of EFFITIX Topical Solution for Dogs

Efficacy Against Fleas: Onset of Action

• **Purpose:** The purpose of the study was to determine how rapidly EFFITIX Topical Solution for Dogs killed fleas after a single treatment application on adult dogs.

• **Methods:** In this study, 16 adult dogs were used. Dogs were randomly assigned to either a control group (6 dogs) or a treatment group (10 dogs). Dogs were housed individually during the course of the study. Twenty-four hours prior to treatment, each dog was infested with 100 unfed adult fleas. Dogs were treated according to label directions. Flea counts were performed at 2, 6, and 12 hours after treatment and geometric mean flea counts per group were calculated.

• **Results:** Flea numbers post treatment were reduced by 32.5% at 2 hours, 94.4% at 6 hours, and by 12 hours, 99.6% of the fleas had been eliminated. The results are provided in Figure 1.

• **Conclusion:** EFFITIX Topical Solution for Dogs kills more than 90% of fleas within 6 hours and more than 99% of fleas within 12 hours following application.

**Figure 1. Speed of killing fleas following treatment with EFFITIX Topical Solution for Dogs**
Efficacy AgainstTicks: Duration of Action

• **Purpose:** The purpose of these studies was to determine the duration of efficacy of EFFITIX Topical Solution for Dogsagainst *Rhipicephalus sanguineus* (brown dog tick), *Dermacentor variabilis* (the American dog tick), *Amblyomma americanum* (the lone star tick), and *Ixodes scapularis* (the blacklegged tick).

• **Methods:** Four studies were conducted, with 12 adult dogs used in each. For each study, dogs were randomly assigned to either a control group (6 dogs) or a treatment group (6 dogs). Dogs were housed individually during the course of the study. Dogs in the *R.* *sanguineus* (brown dog tick) and the *D.* *variabilis* (American dog tick) studies were infested with 50 adult ticks 2 hours prior to treatment. Forty-eight hours after treatment, dogs were combed and ticks counted (Day 2). To evaluate the duration of the killing effect, all dogs were infested weekly from Day 7 to Day 63 with 50 adult *Rhipicephalus* or *Dermacentor* ticks. Tick counts were determined 48 hours after infestation, and geometric mean tick counts per group were calculated.

Dogs in the *A.* *americanum* (lone star tick) study were infested with 50 adult ticks 2 hours prior to treatment. Forty-eight hours after treatment, dogs were combed and ticks counted (Day 2). To evaluate the duration of the killing effect, all dogs were infested weekly from Day 7 to Day 42 with 50 adult *Amblyomma* ticks. Tick counts were determined 48 hours after infestation, and geometric mean tick counts per group were calculated.

Dogs in the *I.* *scapularis* (blacklegged tick) study were infested with 50 adult ticks 2 hours prior to treatment. Forty-eight hours after treatment, dogs were combed and ticks counted (Day 2). To evaluate the duration of the killing effect, all dogs were infested weekly from Day 7 to Day 49 with 50 adult *Ixodes* ticks. Tick counts were determined 48 hours after infestation, and geometric mean tick counts per group were calculated.

• **Results:** By 9 days after treatment, >90% efficacy was achieved against all 4 species of ticks. The duration of >90% efficacy varied by tick species. The results are provided in Figures 2 through 5.

• **Conclusion:** EFFITIX Topical Solution for Dogs kills more than 90% of ticks by 9 days after treatment. Duration of efficacy varied by tick species.
Figure 2. Duration of efficacy of EFFITIX Topical Solution for Dogs against the brown dog tick, *R. sanguineus*

![Graph showing duration of efficacy for *R. sanguineus*](image)

Figure 3. Duration of efficacy of EFFITIX Topical Solution for Dogs against the American dog tick, *D. variabilis*

![Graph showing duration of efficacy for *D. variabilis*](image)
Figure 4. Duration of efficacy of EFFITIX Topical Solution for Dogs against the lone star tick, *A. americanum*

![Graph showing the duration of efficacy against *A. americanum*.](image)

Figure 5. Duration of efficacy of EFFITIX Topical Solution for Dogs against the blacklegged tick, *I. scapularis*

![Graph showing the duration of efficacy against *I. scapularis*.](image)
Water Resistance of EFFITIX Topical Solution for Dogs

Efficacy Against Ticks and Fleas Following Shampooing

• **Purpose:** The purpose of the study was to determine the effect of shampooing and periodic water immersion of dogs on the efficacy of EFFITIX Topical Solution for Dogs against *R. sanguineus* (brown dog tick) and the cat flea.

• **Methods:** Twenty-four dogs were used in this study and were randomly assigned to 1 of 4 groups (containing 6 dogs each):
  - Group 1: control dogs, shampooed on Day 12 and water-immersed on Day 12 and Day 26
  - Group 2: dogs were treated with EFFITIX Topical Solution for Dogs, no shampoo or water immersion
  - Group 3: dogs were treated with EFFITIX Topical Solution for Dogs and shampooed on Day 12
  - Group 4: dogs were treated with EFFITIX Topical Solution for Dogs and water-immersed on Day 12 and Day 26

Dogs were housed individually during the course of the study. Tick infestations (50 ticks per dog) were performed one day prior to treatment and on Days 6, 13, 20, and 27. Flea infestations (100 fleas per dog) were performed on Day 0 (4 h prior to treatment) and on Days 7, 14, 21, and 28. Tick and cat flea counts were performed on Days 2, 9, 16, 23, and 30. Geometric mean tick counts per group were calculated on each day of counting.

Dogs were shampooed with ALLERGROOM® Shampoo. Shampoo was uniformly distributed over the surface of the hair and applied around lips, under the tail, and between the toes. The dog’s body was massaged to develop lather and immediately rinsed after 5 minutes. Dog were towel- or blow-dried.

• **Results:** In dogs in group 2 (treated with EFFITIX Topical Solution for Dogs, not shampooed or immersed in water), EFFITIX Topical Solution for Dogs was 100% effective against fleas and ticks after Day 9. In dogs in group 3 (treated with EFFITIX Topical Solution for Dogs, shampooed on Day 12), EFFITIX Topical Solution for Dogs was 100% effective against fleas after Day 9 and 100% effective against ticks from Day 9 through Day 23, despite the use of a shampoo on Day 12. In dogs in group 4 (treated with EFFITIX Topical Solution for Dogs, immersed in water on Days 12 and 26), EFFITIX Topical Solution for Dogs was 100% effective against fleas and ticks after Day 9. The results are found in Figure 6 and Figure 7.
**Conclusion:** This study showed that use of shampoo or water immersion had no effect on the effectiveness of EFFITIX Topical Solution for Dogs on the brown dog tick (*R. sanguineus*) and on the cat flea in dogs. This study also confirmed that EFFITIX Topical Solution for Dogs is effective for up to a month against the brown dog tick and on the cat flea in dogs.

*Figure 6. Effect of shampooing or water immersion on the efficacy of EFFITIX Topical Solution for Dogs against cat fleas*
Figure 7. Effect of shampooing or water immersion on the efficacy of EFFITIX Topical Solution for Dogs against *R. sanguineus*

Repellency of EFFITIX Topical Solution for Dogs

Repellency Against Ticks

- **Purpose:** The purpose of the study was to determine the repellence efficacy, tick-killing effect, and tick viability impact of EFFITIX Topical Solution for Dogs against *D. variabilis* and *R. sanguineus* in dogs.

- **Methods:** Twelve dogs were used in this study and were randomly assigned to 1 of 2 groups of 6 dogs each. Dogs in group 1 were used as controls, and dogs in group 2 were treated with EFFITIX Topical Solution for Dogs. Dogs were housed individually during the course of the study. Dogs in group 2 were treated one day before tick infestation. Tick infestations (30 ticks of each species per dog) were performed on Days 1, 3, 7, 14, 21, 22, and 28. Tick infestations were performed in infestation chambers on sedated dogs. After a 10-minute exposure time, the dogs were removed from the
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Infestation chambers and the ticks remaining in the chamber were collected and counted. Immediately following the tick’s removal from the infestation chambers, all live ticks were collected and an assessment of their viability was performed over the next 48 hours. Ticks remaining on the dogs were counted by hand 3 hours after the infestation. During these hand counts, ticks were not removed. Ticks were removed and counted 24 hours after infestation on Days 2, 4, 8, 15, 22, 23, and 29.

• Results: For repellency after 10 minutes of exposure, the percentage of repelled ticks varied markedly based on tick species. The level of repellency for *R. sanguineus* ranged from 1.1% to 16.7%, depending on the study day. The level of repellency for *D. variabilis* ranged from 26.6% to 48.0%, depending on the study day. The difference in percentage of repelled ticks in the treated group versus the control group ranged from 26.6% to 48.0%, depending on the study day (Figure 8). Although few *R. sanguineus* ticks were repelled, the viability assessment resulted in variable results, but the majority of the ticks were dead at the viability assessment at 24 hours. The viability assessment of *D. variabilis* ticks showed a higher rate of mortality in ticks within 48 hours during the days following treatment.

Tick counts performed by hand at 3 hours after infestation showed significant tick mortality after each infestation. Efficacies above 88% were seen on Days 3 to 22 for both *R. sanguineus* and *D. variabilis* (Figure 9). Tick counts at 24 hours showed greater than 97% efficacy against *R. sanguineus* and *D. variabilis* throughout the 29-day study period (Figure 10). These results confirmed that EFFITIX Topical Solution for Dogs is effective for at least a month. When the 24-hour tick counts were compared with the tick counts performed at 3 hours, results showed that most tick mortality occurred in the first 3 hours of exposure (approximately 90%).

• Conclusion: EFFITIX Topical Solution for Dogs began to repel ticks within 10 minutes of exposure to the product. The majority of the repelled ticks were dead within 24-48 hours after the initial 10-minute exposure to the treated dog. Ticks that were not repelled were killed by 1 day after infestation. Most of these ticks were killed within the first 3 hours after exposure to the treated dog.
Figure 8. Repellence efficacy of EFFITIX Topical Solution for Dogs against *R. sanguineus* and *D. variabilis*

<table>
<thead>
<tr>
<th>DAYS AFTER TREATMENT</th>
<th>Ticks Repelled after 10 Minutes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.1 (R. sanguineus) 29.1 (D. variabilis)</td>
</tr>
<tr>
<td>3</td>
<td>2.5 (R. sanguineus) 35.8 (D. variabilis)</td>
</tr>
<tr>
<td>7</td>
<td>16.7 (R. sanguineus) 47.4 (D. variabilis)</td>
</tr>
<tr>
<td>14</td>
<td>5.4 (R. sanguineus) 34.6 (D. variabilis)</td>
</tr>
<tr>
<td>21</td>
<td>1.1 (R. sanguineus) 26.6 (D. variabilis)</td>
</tr>
<tr>
<td>22</td>
<td>3.3 (R. sanguineus) 29.3 (D. variabilis)</td>
</tr>
<tr>
<td>28</td>
<td>6.4 (R. sanguineus) 48 (D. variabilis)</td>
</tr>
</tbody>
</table>
Figure 9. Efficacy of EFFITIX Topical Solution for Dogs against \textit{R. sanguineus} and \textit{D. variabilis} 3 hours after infestation.
Figure 10. Efficacy of EFFITIX Topical Solution for Dogs against R. sanguineus and D. variabilis 24 hours after infestation

Efficacy of EFFITIX Topical Solution for Dogs Against Mosquitoes

Duration of Efficacy Against Mosquitoes:

- **Purpose:** The purpose of the study was to assess the efficacy of a single application of EFFITIX Topical Solution for Dogs against mosquitoes (Aedes aegypti) on dogs.

- **Methods:** Twelve dogs were used in this study and randomly assigned to 1 of 2 treatment groups of 6 dogs each. Dogs in group 1 were used as control and dogs in group 2 were treated with EFFITIX Topical Solution for Dogs. Each group contained 2 long-haired dogs and 4 short-haired dogs. Dogs were housed individually during the course of the study. Dogs were exposed to mosquitoes on Days 1, 7, 14, 21, 28, and 35 as follows: after sedation, dogs were placed into individual mosquito cages and exposed for 30 minutes to 100+/10 female mosquitoes (A. aegypti) of at least 2 days old. Afterwards mosquitoes were collected, dogs were removed from the cage, and dead and alive mosquitoes were counted at 60 minutes post exposure. Then mosquitoes were frozen and crushed to determine if any had taken blood meals. Fed and unfed mosquitoes were counted.
• **Results:** The study showed a moderate killing effect of mosquitoes, particularly in the short-haired dogs. A killing effect around 40% to 50% for up to 28 days was observed in this group. The anti-feeding efficacy of the product was more consistent in the short-haired dogs. The anti-feeding efficacy was >77% for 28 days.

• **Conclusion:** EFFITIX Topical Solution for Dogs provided dogs substantial anti-feeding effects against mosquitoes for 28 days. This anti-feeding effect can provide an additional benefit to reduce the risk of the transmission of heartworm infection, especially in dogs in heartworm-endemic areas.

**Tolerance of EFFITIX Topical Solution for Dogs**

**Tolerance in Adult Dogs**

• **Purpose:** The purpose of the study was to evaluate the tolerance to EFFITIX Topical Solution for Dogs in adult dogs at 1x and 5x the normal dose of EFFITIX Topical Solution for Dogs.

• **Study design:** In this study, 36 healthy adult Beagle dogs were randomly assigned to 3 groups, each containing 6 male and 6 female dogs. The ages of the dogs ranged from 9–10 months and the weight ranged from 22–32 lbs. The 3 groups were treated in the following manner:
  • Group 1: dogs were the control group and treated with a placebo
  • Group 2: dogs were treated with the normal dose of EFFITIX Topical Solution for Dogs
  • Group 3: dogs were treated with 5x the normal dose of EFFITIX Topical Solution for Dogs

Following treatment, dogs were evaluated hourly for 8 hours after treatment and twice daily for the following 14 days. The following physical and clinical measures were measured during the study: body weight, food consumption, blood parameters, and clinical evaluations.
• **Results:** Dogs in all treatment groups ate normally and maintained weight throughout the duration of the study. No clinically important abnormalities were noted in blood cell counts or in blood chemistries. No treatment-related clinical signs were observed in the group treated at 1x the normal dose. Loose feces were observed in 3 of the dogs in the group treated at 5x the normal dose 8–12 hours after administration. Loose feces were also observed in all groups occasionally during the 14-day observation period. There was no evidence of any skin reactions at the dosage sites in any dogs.

• **Conclusion:** The tolerance of EFFITIX Topical Solution for Dogs was evaluated in an overdose safety study using adult Beagle dogs. No detrimental effects were noted in any dogs. EFFITIX Topical Solution for Dogs was well tolerated, both locally and systemically in adult dogs.

How to Handle Adverse Reactions

• **What to do if there is a reaction:** If an unexpected sign occurs within 24–48 hours of treatment, it is recommended to bathe the dog with a degreasing liquid dish detergent (Dawn® or Palmolive®), which will remove most of the product. Follow with symptomatic and supportive treatment. Please call Virbac Animal Health for further advice.

• **Misapplication of EFFITIX Topical Solution for Dogs to a cat:** EFFITIX Topical Solution for Dogs contains permethrin and should only be used on dogs and never used on cats. Exposure in cats can be harmful and even deadly due to their unique physiology and inability to metabolize certain compounds. Cats may be exposed if the product is accidentally applied directly to them or through direct ingestion (eg, the cat grooms the wet product off of a dog). In mixed households, care should be taken to separate cats from dogs until product is dry. Signs of EFFITIX Topical Solution for Dogs toxicosis in cats can include tremors, drooling, lack of appetite, vomiting, diarrhea, incoordination, hyperactivity, disorientation, vocalization, depression, difficulty breathing, and seizures. Death is possible if not treated appropriately and immediately.
• If a cat is accidentally administered EFFITIX Topical Solution for Dogs or if it is exposed to EFFITIX Topical Solution for Dogs from a treated dog and signs are evident, the following is recommended:

1. If administered directly to a cat, the cat should be bathed with a degreasing liquid dish detergent (Dawn or Palmolive) to remove any residual product. Dry the cat well and maintain body temperature.

2. If the cat begins to show clinical signs, it will need to be treated. Tremors can be controlled with methocarbamol injectable administered intravenously. Seizures will need to be controlled, and the cat will need to be put on fluids to maintain hydration and nutrition.

3. Recovery is usually within 24–72 hours if treated appropriately.

4. You should recommend that the veterinarian call Virbac Animal Health at 800-338-3659 to report.

• **Hazards to domestic animals—for external use on dogs ONLY.** Do not use on dogs under 12 weeks of age. Individual sensitivities, while rare, may occur after using ANY pesticide product. Dogs may experience some temporary irritation at the site of product application. If signs of sensitivity occur, bathe the dog with mild soap or shampoo and rinse with large amounts of water.

• **DO NOT USE ON CATS OR RABBITS**

• **For external use on dogs ONLY.** Do not use on dogs under 12 weeks of age. Do not split tubes between dogs. Do not use multiple tubes on one dog. Weigh the dog to be sure you are applying the right dose formulated for the weight of the dog. Overdosing a dog can result in serious illness. Do not bathe the dog within the first 24 hours after the product has been applied. Do not apply more often than once per month (every 30 days).
HAZARDS TO HUMANS
Harmful if swallowed and causes eye irritation. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

• **First Aid**
  **If swallowed:**
  • Call a poison control center or doctor immediately for treatment advice.
  • Have person sip a glass of water if able to swallow.
  • Do not induce vomiting unless told to do so by a poison control center or doctor.
  • Do not give anything by mouth to an unconscious person.

  **If in eyes:**
  • Hold eye open and rinse slowly and gently with water for 15–20 minutes.
  • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.
  • Call a poison control center or doctor for treatment advice.

  **If on skin or clothing:**
  • Take off contaminated clothing.
  • Rinse skin immediately with plenty of water for 15–20 minutes.
  • Call a poison control center or doctor for treatment advice.
EFFIPRO® Topical Solution for Cats

EFFIPRO Topical Solution for Cats is a fipronil-based product from Virbac Animal Health for use in cats and kittens. EFFIPRO Topical Solution for Cats has equal efficacy against fleas when compared to FRONTLINE®. Following application, EFFIPRO Topical Solution for Cats has residual parasite-killing properties over the 28-day treatment interval.

Product Description and Dosing

KEEP OUT OF REACH OF CHILDREN

• **Indication:** EFFIPRO Topical Solution for Cats is indicated for CATS and KITTENS (8 weeks old or older) to control fleas, ticks (brown dog tick, American dog tick, lone star tick, and deer tick), and chewing lice.

• **Hazards to Humans:** Harmful if swallowed and causes eye irritation. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

• **Hazards to Domestic Animals:** For external use on cats ONLY. Do not use on kittens under 8 weeks of age. Individual sensitivities, while rare, may occur after using ANY pesticide product. Possible temporary irritation may occur at the site where EFFIPRO Topical Solution for Cats was applied. Contact a veterinarian immediately if signs become persistent or become more severe during the first few days following application. If an unusual reaction is observed following initial application, a veterinarian should be consulted before repeating treatment. Certain medications can interact with pesticides. Consult a veterinarian before using on medicated, debilitated, or aged animals.

• **DO NOT USE ON RABBITS.**

• **Directions for Use:** For external use on cats ONLY. Do not use on kittens under 8 weeks of age.

• **Active Ingredients:** Fipronil. EFFIPRO Topical Solution for Cats contains 9.6% fipronil on a by-weight basis.

• **Packaging:** EFFIPRO Topical Solution for Cats is packaged as plastic dispensing applicators that are available in 1-, 3-, 6-, and 36-dose packs. One dose size (0.017 fl oz, 0.5 mL) treats all sizes of cats.
• **Storage Conditions:** Store in original container only, out of reach of children and animals.

• **Application Directions:**
  1. Remove one applicator from packaging. Hold applicator upright and remove cap.
  2. Invert cap and place other end back onto applicator tip. Push cap down to break seal. Remove cap prior to treatment application.
  3. Part cat's hair between shoulder blades until skin is visible. Place applicator tip directly against exposed skin. Deposit entire contents by squeezing the applicator at a single site on cat’s skin. Ensure that EFFIPRO Topical Solution for Cats is not applied superficially on cat’s hair.

• **Frequency of Application:** EFFIPRO Topical Solution for Cars will kill fleas, ticks, and chewing lice completely when applied monthly.

• **Fleas:** EFFIPRO Topical Solution for Cats can control fleas for up to 6 weeks. Apply monthly if your cat has fleas that may cause flea allergy dermatitis or if reinfestation is likely.

• **Ticks:** EFFIPRO Topical Solution for Cats can kill ticks for a month or longer. Apply monthly where tick control is consistently needed.
Technical Profile

Product Features and Benefits

<table>
<thead>
<tr>
<th>Feature</th>
<th>Advantage</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Versatility in dispensing with 4 presentation sizes</td>
<td>1-dose and 36-dose packages are available in addition to the traditional 3-dose and 6-dose presentations</td>
<td>The 1-dose package provides veterinarians with an EPA-approved option for selling product on a month-to-month basis. The 1-dose package also presents an opportunity for monthly home delivery. The 36-dose package is great for sampling</td>
</tr>
<tr>
<td>Quick acting</td>
<td>Starts killing adult fleas within 6 hours</td>
<td>Quickly kills fleas that may cause flea allergy dermatitis</td>
</tr>
<tr>
<td>Virbac’s international experience</td>
<td>Over 3 years of international experience selling fipronil-based products</td>
<td>You can buy from a company with experience manufacturing and supporting fipronil-based products</td>
</tr>
<tr>
<td>A company you can trust</td>
<td>Virbac Animal Health is the largest company in the world that is dedicated only to the animal health industry</td>
<td>Veterinarians can buy from a company that partners with veterinarians</td>
</tr>
</tbody>
</table>

Efficacy Study of EFFIPRO Topical Solution for Cats

Duration of Action Against Fleas

- **Purpose:** The purpose of the study was to determine the efficacy of EFFIPRO Topical Solution for Cats following a single treatment on cats.
• **Methods:** 18 adult cats were used in this study. Cats were randomly assigned to 1 of 3 groups of 6 cats each. Cats in group 1 were used as control cats, cats in group 2 were treated with FRONTLINE® Top Spot®, and cats in group 3 were treated with EFFIPRO Topical Solution for Cats. Cats were housed individually during the course of the study. Twenty-four hours prior to treatment, each cat was infested with 100 adult unfed fleas. Cats were treated according to manufacturer’s instructions. Flea counts were performed on 2 days after treatment. On Days 7, 14, 21, 28, 35, and 42, cats were reinfested with 100 adult unfed flea and flea counts were performed 48 hours after reinestation on Days 9, 16, 23, 30, 37, and 44. Geometric mean flea counts per group were calculated on each day of counting.

• **Results:** FRONTLINE Top Spot was 100% efficacious against fleas through Day 16 and 99.6% efficacious on Day 23. Efficacy for FRONTLINE dropped to 76.0%, 79.5%, and 75.0% on Days 30, 37, and 44, respectively. EFFIPRO Topical Solution for Cats was 100% efficacious through Day 30. Efficacy for EFFIPRO Topical Solution for Cats dropped to 86.4% on Day 37 and to 78.4% on Day 44. The results are provided in Figure 11.

• **Conclusion:** Efficacy of EFFIPRO Topical Solution for Cats against fleas was equal to FRONTLINE throughout the duration of the study.

Figure 11. Duration of efficacy of EFFIPRO Topical Solution for Cats
Tolerance of EFFIPRO Topical Solution for Cats

How to Handle Adverse Reactions

• **What to do if there is a reaction:** If an unexpected sign occurs within 24–48 hours of treatment, it is recommended to bathe the cat with a degreasing liquid dish detergent (Dawn® or Palmolive®), which will remove most of the product. Follow with symptomatic and supportive treatment. Please call Virbac Animal Health for further advice.

• **Hazards to domestic animals—**for external use in cats ONLY. Do not use on kittens under 8 weeks of age. Individual sensitivities, while rare, may occur after using ANY pesticide product. Possible temporary irritation may occur at the site where EFFIPRO Topical Solution for Cats was applied.

• **DO NOT USE ON RABBITS**

HAZARDS TO HUMANS

Harmful if swallowed and causes eye irritation. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

• **First Aid**

  **If swallowed:**
  • Call a poison control center or doctor immediately for treatment advice.
  • Have person sip a glass of water if able to swallow.
  • Do not induce vomiting unless told to do so by a poison control center or doctor.
  • Do not give anything by mouth to an unconscious person.

  **If in eyes:**
  • Hold eye open and rinse slowly and gently with water for 15–20 minutes.
  • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.
  • Call a poison control center or doctor for treatment advice.

  **If on skin or clothing:**
  • Take off contaminated clothing.
  • Rinse skin immediately with plenty of water for 15–20 minutes.
  • Call a poison control center or doctor for treatment advice.
Appendix A: Medical Importance of Fleas

The medical importance of fleas results from:

1. Their broad distribution and the high prevalence of infestation in dogs and cats
2. Their high potential for proliferation
3. Their ability to induce clinical signs on host as well as transmit diseases

The Broad Distribution of the Cat Flea

Flea infestation is one of the most frequent ectoparasitic conditions of dogs and cats. There are more than 2,000 species and sub-species of fleas distributed throughout the world. Only a few infest dogs and cats: *Ctenocephalides felis* (the cat flea), *Ctenocephalides canis* (the dog flea), *Echidnophaga gallinacea* (the sticktight flea), and *Pulex simulans* (the mammal flea).

By far the most prevalent flea infesting both dogs and cats is *Ctenocephalides felis*. In a survey performed between 1996 and 2004 in Georgia on dogs, 2,518 fleas were collected and 5 species were identified. The cat flea, *C. felis*, was the most prevalent (61% of fleas), followed by the dog flea (21% of fleas), the mammal flea (13% of fleas), the sticktight flea (4% of fleas), and the eastern rabbit flea (*Cediopsylla simplex*, 1% of fleas).

High Potential for Proliferation

The flea completes its life cycle through a number of stages, beginning with the egg laid on the host that subsequently falls on the ground/floor and from which the larva emerges, developing into a pupa, the resistant stage, and finally the adult. Under the correct environmental conditions, completion of the cycle takes 2–4 weeks and can be prolonged up to 140 days, depending on temperature and humidity notably.

Once on the host, the adult flea takes the first blood meal within minutes and mating occurs subsequently. The eggs are laid on the pet within 24 hours of feeding. **On average, a female flea will lay 27 eggs a day over 50 days (1,350 eggs).** About 40% of eggs will develop up to the adult stage.
Diseases Related to Flea Infestation
The flea can be a direct or indirect cause of medical disorders in pets and their owners.

- **Pulicosis and Flea Anemia**
  Flea bites cause skin irritation and pruritus in small animals. Pruritus due to simple *C. felis* infestation is usually mild. Female fleas consume 15 times their weight in blood each day. In dogs and cats with heavy flea infestations, the continuous loss of blood can produce an iron deficiency anemia. Healthy adult dogs and cats have the body reserves to withstand the effects of this anemia. However, in puppies and kittens with limited body reserves, heavy infestations can result in severe anemia and death. Debilitated older pets, especially cats, are also at risk of developing severe anemia because of their lack of appetite and food consumption and their disinterest in or inability to groom and mechanically remove the fleas.

- **Flea Allergy Dermatitis (FAD)**
  In individuals hypersensitive to flea bites, severe pruritus and resulting self-inflicted lesions may result from flea infestation, leading to the dermatological condition called FAD. Hypersensitivity is provoked by flea saliva, which contains a cocktail of histamine-like compounds, enzymes, polypeptides, and amino acids.

- **Tapeworm**
  Cat fleas serve as intermediate hosts for the common intestinal tapeworm of dogs and cats, *Dipylidium caninum*. Flea larvae ingest the eggs of the tapeworm, which develop into cysticercoids in the body of the flea. Dogs and cats may ingest infected fleas when grooming, releasing cysticercoids in their intestinal tract. This tapeworm can infect humans and particularly children interacting with pets after accidental ingestion of infected fleas.

- **Flea-Borne Diseases**
  Flea bites can spread pathogenic organisms between cats. Some of these microorganisms may threaten the health of humans and animals. Examples of diseases that fleas transmit include bartonellosis ("cat scratch disease," causing swelling of the lymph nodes in humans) and hemoplasmosis (formerly called hemobartonellosis, which can cause severe anemia in cats).
Appendix B: Medical Importance of Ticks

The medical importance of ticks mainly results from their role as vectors of various diseases and their broad distribution in the environment.

The Broad Distribution of Ticks

Ticks are blood feeders almost distributed worldwide. Approximately 850 tick species have been described. The family Ixodidae is by far the largest and most important economically and includes 13 genera and approximately 650 species. The most significant hard ticks in North America that feed on companion animals include:

- *Ixodes* spp. (*I. scapularis, I. pacificus*)
- *Rhipicephalus* spp. (*R. sanguineus*)
- *Dermacentor* spp. (*D. variabilis, D. andersoni*)
- *Amblyomma* spp. (*A. americanum, A. maculatum*)

All of these ticks are “3-host ticks” and have a very similar life cycle, requiring 3 separate feedings on 3 animals during their lifetime.

Ticks Are Major Vectors of Pathogenic Agents

All active stages of the tick life cycle require blood as a nutrient source and, in the case of adults, for sperm or egg production. The life cycle of ticks includes 4 stages, the embryonated egg and 3 active stages: the larva, the nymphal stage(s), and the adult.

The consequences of tick bites per se generally are not serious. An inflammatory reaction often occurs around the feeding site and complications can be seen after incomplete tick removal (inflammatory granuloma lasting several weeks, abscess). A list of the common tick transmitted diseases is found Table 2.
Table 2. Diseases Transmitted by Ticks

<table>
<thead>
<tr>
<th>Infectious agent/ bacterial agent</th>
<th>Disease</th>
<th>Vector</th>
<th>Species involved</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Anaplasma phagocytophilum</em></td>
<td>Canine and feline granulocytotropic anaplasmosis</td>
<td><em>Ixodes</em></td>
<td>Dog, horse, cat, human</td>
</tr>
<tr>
<td><em>Anaplasma platys</em></td>
<td>Thrombocytotropic anaplasmosis</td>
<td><em>Rhipicephalus, Dermacentor suspected</em></td>
<td>Dog</td>
</tr>
<tr>
<td><em>Babesia canis</em></td>
<td>Babesiosis</td>
<td><em>Rhipicephalus, Dermacentor</em></td>
<td>Dog, cat uncommon but possible</td>
</tr>
<tr>
<td><em>Borrelia burgdorferi</em></td>
<td>Lyme disease, canine borreliosis</td>
<td><em>Ixodes, Rhipicephalus suspected</em></td>
<td>Dog, cat, human</td>
</tr>
<tr>
<td><em>Ehrlichia canis</em></td>
<td>Canine and feline monocytotropic ehrlichiosis</td>
<td><em>Rhipicephalus, Dermacentor</em></td>
<td></td>
</tr>
<tr>
<td><em>Ehrlichia chaffensis</em></td>
<td>Human monocytotropic ehrlichiosis</td>
<td><em>Amblyomma</em></td>
<td>Dog, cat, human</td>
</tr>
<tr>
<td><em>Ehrlichia ewingii</em></td>
<td>Canine granulocytotropic ehrlichiosis</td>
<td><em>Amblyomma, Dermacentor, Rhipicephalus suspected</em></td>
<td>Dog, human</td>
</tr>
<tr>
<td><em>Francisella tularensis</em></td>
<td>Tularemia</td>
<td><em>Dermacentor</em></td>
<td>Dog, cat</td>
</tr>
<tr>
<td><em>Hepatozoon spp.</em></td>
<td>Canine and feline hepatozoonosis</td>
<td><em>Amblyomma, Rhipicephalus</em></td>
<td>Dog, cat</td>
</tr>
<tr>
<td><em>Mycoplasma haemocanis</em> (Hemobartonella canis)</td>
<td>Hemobartonellosis</td>
<td><em>Ixodes, Rhipicephalus</em></td>
<td>Dog, cat</td>
</tr>
<tr>
<td><em>Rickettsia rickettsia</em></td>
<td>Rocky Mountain spotted fever (potentially fatal)</td>
<td><em>Dermacentor, Rhipicephalus</em></td>
<td>Dog, human</td>
</tr>
</tbody>
</table>
EFFITIX Topical Solution for Dogs

How long does EFFITIX Topical Solution for Dogs remain active after application?
Clinical studies demonstrate that EFFITIX Topical Solution for Dogs maintains its efficacy for the full 30 days after application.

How often does EFFITIX Topical Solution for Dogs need to be reapplied? Does it need to be administered year-round?
EFFITIX Topical Solution for Dogs should be applied monthly. The Companion Animal Parasite Council (CAPC) recommends year-round application of tick-control products because of the substantial geographic differences that occur in tick prevalence and seasonality.

What is the minimum age in dogs when using EFFITIX Topical Solution for Dogs?
EFFITIX Topical Solution for Dogs should be used on dogs ≥ 12 weeks of age.

Can EFFITIX Topical Solution for Dogs be used in pregnant, lactating, or breeding dogs?
EFFITIX Topical Solution for Dogs has not been tested on these types of animals. EFFITIX Topical Solution for Dogs should not be used on pregnant, nursing, or breeding dogs unless directed by a veterinarian.

Are there any drug interactions or contraindications with the use of EFFITIX Topical Solution for Dogs (eg, chronic medications such as RIMADYL®, phenobarbital, SOLOXINE®)?
Although the components of EFFITIX Topical Solution for Dogs have been used in dogs concurrently medicated with other drugs, EFFITIX Topical Solution for Dogs has not been tested on these types of animals. EFFITIX Topical Solution for Dogs should not be used on debilitated, aged, or medicated dogs or dogs known to be sensitive to pesticide products unless directed by a veterinarian.

Does EFFITIX Topical Solution for Dogs have an odor?
No, EFFITIX Topical Solution for Dogs is an odorless yellowish liquid.
Does EFFITIX Topical Solution for Dogs produce a greasy or oily appearance to the hair coat once it is applied? How long will the greasy appearance last?

Like all topically applied products, deposits, clumping or spiking of the fur, or a greasy appearance can be seen at the application site. These are cosmetic issues and do not affect the efficacy of the product. The degree to which these occur and their duration depend on the hair coat length and coarseness of hair.

How does the volume of EFFITIX Topical Solution for Dogs compare to other topical products?

The quantities of fipronil and permethrin in EFFITIX Topical Solution for Dogs required to ensure good efficacy against parasites requires some additional dose volume when compared to FRONTLINE PLUS®. However, the volume of EFFITIX Topical Solution for Dogs is slightly less than that found in CERTIFECT™, Merial’s new fipronil/amitraz combination product.

<table>
<thead>
<tr>
<th>Dose</th>
<th>EFFITIX™ Topical Solution for Dogs</th>
<th>FRONTLINE PLUS®</th>
<th>CERTIFECT™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 22.9 lbs</td>
<td>1 mL</td>
<td>0.67 mL</td>
<td>1.07 mL</td>
</tr>
<tr>
<td>23.0–44.9 lbs</td>
<td>2 mL</td>
<td>1.34 mL</td>
<td>2.14 mL</td>
</tr>
<tr>
<td>45.0–88.9 lbs</td>
<td>4 mL</td>
<td>2.68 mL</td>
<td>4.28 mL</td>
</tr>
<tr>
<td>89.0–132.0 lbs</td>
<td>6 mL</td>
<td>4.02 mL</td>
<td>6.42 mL</td>
</tr>
</tbody>
</table>

How long does it take for EFFITIX Topical Solution for Dogs to start killing fleas and ticks?

Speed of kill studies have shown that EFFITIX Topical Solution for Dogs kills >90% of fleas by 6 hours and >99% by 12 hours after application. EFFITIX Topical Solution for Dogs begins killing ticks within 3 hours of application with >97% tick mortality within 24 hours of application.
How long does it take for EFFITIX Topical Solution for Dogs to dry following application?
The drying time of EFFITIX Topical Solution for Dogs depends on the hair coat length and coarseness of hair. The longer and finer the hair coat, the longer it will take for EFFITIX Topical Solution for Dogs to dry. In general, the product should be dry by 24 hours after application.

Is there any systemic absorption of the active ingredients in EFFITIX Topical Solution for Dogs?
In animals with healthy, intact skin, there is no absorption of the active ingredients in EFFITIX Topical Solution for Dogs. Both fipronil and permethrin remain on the surface of the dog’s skin. Fipronil is found in the lipid layer on the surface of the skin and permethrin is bound tightly to the hair shafts.

Can a dog be bathed before or after EFFITIX Topical Solution for Dogs is applied? If so, how long to wait before or after bathing and product application?
Dogs should not be bathed within 24 hours before and 24 hours after the application of EFFITIX Topical Solution for Dogs. Fipronil requires the lipid layer on the skin to diffuse across the surface of the dog. Removing this lipid layer by bathing either before or after treatment may decrease the efficacy of EFFITIX Topical Solution for Dogs. By 24 hours after application, the fipronil has diffused to the hair follicles and sebaceous glands and permethrin has bound to the hair shafts. Bathing with ALLERGROOM® Shampoo 24 hours after application does not affect the efficacy of EFFITIX Topical Solution for Dogs. Drying time is dependant upon hair coat length and environmental conditions and may take anywhere from 24–48 hours to dry. It is recommended to wait 48 hours before allowing children to come in contact with a treated dog. Degreasing soaps or shampoos may decrease the efficacy of the product because they removed the lipid layer on the skin.

Does EFFITIX Topical Solution for Dogs wash off with swimming?
Swimming 24 hours after application does not affect the efficacy of EFFITIX Topical Solution for Dogs.
How often should EFFITIX Topical Solution for Dogs be applied if the dog is a frequent swimmer or gets weekly baths?
Bathing with a mild shampoo such as ALLERGROOM® Shampoo or swimming does not affect the efficacy of EFFITIX Topical Solution for Dogs. EFFITIX Topical Solution for Dogs should be applied monthly. Degreasing soaps or shampoos may decrease the efficacy of the product.

Are there any shampoos that will “strip” EFFITIX Topical Solution for Dogs off the skin surface?
Degreasing soaps (such as Dawn® dishwashing soap) or shampoos can be used to remove EFFITIX Topical Solution for Dogs from the surface of the skin, especially if used within 24 hours after product application.

What common side effects may be seen in dogs with the use of EFFITIX Topical Solution for Dogs?
Individual sensitivities, while rare, may occur after using ANY pesticide product. Dogs may experience some temporary irritation at the site of product application, including redness, twitching, itching, and scratching. If signs of sensitivity occur, the dog should be bathed with a degreasing soap or shampoo and rinsed with large amounts of water.

What side effects are seen in cats that are accidentally exposed dermally and orally to EFFITIX Topical Solution for Dogs?
Because of their unique physiology and inability to metabolize permethrin, cats can be harmed by the application of EFFITIX Topical Solution for Dogs. Cats can become toxic with ingestion of small amount of the compound. Cats may be exposed if the EFFITIX Topical Solution for Dogs is accidentally applied directly to them, or through direct ingestion (eg, the cat grooms the wet product off of the dog). In mixed households, care should be taken to separate cats from dogs until EFFITIX Topical Solution for Dogs is dry. Signs of toxicosis related to EFFITIX Topical Solution for Dogs in cats can include tremors, drooling, lack of appetite, vomiting, diarrhea, incoordination, hyperactivity, disorientation, vocalization, depression, difficulty breathing, and seizures. Death is possible if not appropriately treated.
Technical Profile: Frequently Asked Questions

Will EFFITIX Topical Solution for Dogs turn a dog’s hair coat a different color when applied?
All topical products applied to dogs have the potential to change hair coat color. The most common color change is seen in dogs with blond or buff coats. In these dogs, the hair coat will become darker at the sight of application. These dark areas will fade with time. No changes are expected to be seen to the skin surface.

What side effects are seen if a dog licks or ingests EFFITIX Topical Solution for Dogs?
Both fipronil and permethrin are minimally toxic to dogs in the levels found in EFFITIX Topical Solution for Dogs. Signs depend on the amount of product ingested and size of dog. Vomiting and salivation are the most commonly reported signs reported in dogs that ingest fipronil- or permethrin-containing products. Neurologic signs (ataxia, tremors, twitching) can be seen if large quantities are ingested, especially in small-breed dogs. Dogs fed 0.2 mg/kg/day fipronil showed no signs of toxicosis. In the same study, clinical signs of neurotoxicity (convulsions, twitching, tremors, ataxia, unsteady gait, rigidity of limbs, nervous behavior, hyper- or hypoactivity, vocalization, nodding, aggression, resistance to dosing and inappetence) were observed at 2.0 mg/kg/day. The no-adverse-effect-level (NOAEL) for fipronil in dogs was determined to be 0.3 mg/kg body weight per day. Dogs fed daily doses of permethrin 500 mg/kg body weight per day showed transient signs of permethrin toxicosis including tremors. The NOAEL for permethrin in dogs was determined to be 50 mg/kg body weight per day.

Can EFFITIX Topical Solution for Dogs be used with other oral parasite preventatives (ie, CAPSTAR®, COMFORTIS®, TRIFEXIS™)?
The listed medications work through a different mechanism of action than those found in EFFITIX Topical Solution for Dogs. To date, EFFITIX Topical Solution for Dogs has not been tested on animals treated with these medications.
Can EFFITIX Topical Solution for Dogs be used with other topical parasite control products or skin treatments (ALLERDERM® Spot-on, ADVANTAGE MULTI®, REVOLUTION®)? If so, how long to wait between applications of the 2 products?

EFFITIX Topical Solution for Dogs should not be used with topical parasite preventatives that contain fipronil or permethrin. To date, EFFITIX Topical Solution for Dogs has not been tested on animals treated with these medications.

Can the product be used with veterinary-branded tick collars?

EFFITIX Topical Solution for Dogs should not be used with SCALIBOR® or any other collars that contain pyrethroids or fipronil. To date, EFFITIX Topical Solution for Dogs has not been tested on animals treated with these medications, so it is important to consult a veterinarian before using EFFITIX Topical Solution for Dogs with any medication.

Can people or children pet or handle the dog after treatment with EFFITIX Topical Solution for Dogs?

Adults and children should avoid contact with EFFITIX Topical Solution for Dogs immediately after it is applied. Once EFFITIX Topical Solution for Dogs is dry on the skin of the dog, people can handle or pet the dog. Drying time is dependent upon hair coat length and environmental conditions and may take anywhere from 24–48 hours to dry. It is recommended to wait until product is dry before allowing children to come in contact with a treated dog.
EFFIPRO Topical Solution for Cats

How long does EFFIPRO Topical Solution for Cats remain active after application?
Clinical studies demonstrate that EFFIPRO Topical Solution for Cats maintains its efficacy for the full 30 days after application.

How often does EFFIPRO Topical Solution for Cats need to be reapplied? Does it need to be administered year-round?
EFFIPRO Topical Solution for Cats should be applied monthly. The CAPC recommends year-round application of tick-control products because of the substantial geographic differences that occur in tick prevalence and seasonality.

What are the minimum age and weight requirements in cats when using EFFIPRO Topical Solution for Cats?
EFFIPRO Topical Solution for Cats is safe to use on cats and kittens ≥8 weeks of age. There is no minimum weight restriction for EFFIPRO Topical Solution for Cats.

Is EFFIPRO Topical Solution for Cats safe to use in pregnant, lactating, or breeding cats?
Yes. EFFIPRO Topical Solution for Cats is approved for use in pregnant, lactating, and breeding cats.

Are there any drug interactions or contraindications with the use of EFFIPRO Topical Solution for Cats (eg, chronic medications such as methimazole)?
Although the components of EFFIPRO Topical Solution for Cats have been used safely in cats concurrently medicated with other drugs, EFFIPRO Topical Solution for Cats has not been tested on these types of animals. EFFIPRO Topical Solution for Cats should not be used on debilitated, aged or medicated dogs or cats known to be sensitive to pesticide products unless directed by a veterinarian.

Does EFFIPRO Topical Solution for Cats have an odor?
No, EFFIPRO Topical Solution for Cats is an odorless yellowish liquid.
Does EFFIPRO Topical Solution for Cats produce a greasy or oily appearance to the hair coat once it is applied? How long will the greasy appearance last?

Like all topically applied products, deposits, clumping or spiking of the fur, or a greasy appearance can be seen at the application site. These are cosmetic issues and do not affect the efficacy of the product. The degree to which these occur and their duration depend on the hair coat length and coarseness of hair.

How does the volume of EFFIPRO Topical Solution for Cats compare to other topical products?

EFFIPRO Topical Solution for Cats contains 0.5 mL of solution and is comparable in volume to both FRONTLINE® Top Spot® and FRONTLINE PLUS®. Both contain 0.67 mL solution.

How long does it take for EFFIPRO Topical Solution for Cats to start killing fleas and ticks?

Speed of kill studies have shown that EFFIPRO Topical Solution for Cats kills >90% of fleas by 6 hours and >99% by 12 hours after application. EFFIPRO Topical Solution for Cats begins killing ticks within 3 hours of application with >97% tick mortality within 24 hours of application.

How long does it take for EFFIPRO Topical Solution for Cats to dry following application?

The drying time of EFFIPRO Topical Solution for Cats depends on the hair coat length and coarseness of hair. The longer and finer the hair coat, the longer it will take for EFFIPRO Topical Solution for Cats to dry. In general, the product should be dry by 24 hours after application. Drying time is dependent upon hair coat length and environmental conditions and may take anywhere from 24–48 hours to dry. It is recommended to wait until product is dry before allowing children to come in contact with a treated cat.

Is there any systemic absorption of the active ingredients in EFFIPRO Topical Solution for Cats?

In cats with healthy intact skin, there is no absorption of the active ingredients in EFFIPRO Topical Solution for Cats. Fipronil remains on the surface of the cat’s skin. Fipronil is found in the lipid layer on the surface of the skin.
Technical Profile: Frequently Asked Questions

Are there any precautions with the use of EFFIPRO Topical Solution for Cats in species other than cats?
Do not use on rabbits. Fipronil is considered toxic to birds in the family Galliformes (turkeys, chickens, grouse, quail, pheasants, partridges) and both fipronil and permethrin are toxic to a number of fish and aquatic species.

What common side effects can be expected in cats with the use of EFFIPRO Topical Solution for Cats?
Individual sensitivities, while rare, may occur after using ANY pesticide product. Cats may experience temporary irritation at the site of product application.

What side effects can be seen if a cat licks or ingests EFFIPRO Topical Solution for Cats?
Fipronil is minimally toxic to cats in the levels found in EFFIPRO Topical Solution for Cats. Signs depend on the amount of product ingested and size of cat. Vomiting and salivation are the most commonly reported signs reported in cats that ingest fipronil-containing products. Neurologic signs (ataxia, tremors, twitching) can be seen if large quantities are ingested.

Can EFFIPRO Topical Solution for Cats be used with other oral parasite preventives (ie, CAPSTAR®)?
These medications work through a different mechanism of action than those found in EFFIPRO Topical Solution for Cats. To date, EFFIPRO Topical Solution for Cats has not been tested on animals treated with these medications.

Can EFFIPRO Topical Solution for Cats be used with other topical treatments (eg, ADVANTAGE MULTI®, REVOLUTION®)? If so, how long to wait between applications of the 2 products?
EFFIPRO Topical Solution for Cats should not be used with topical parasite preventatives that contain fipronil. To date, EFFIPRO Topical Solution for Cats has not been tested on animals treated with these medications.

Can people or children pet or handle the cat after treatment with EFFIPRO Topical Solution for Cats?
Adults and children should avoid contact with the cat immediately after application of EFFIPRO Topical Solution for Cats. Once EFFIPRO Topical Solution for Cats is dry on the skin of the cat, people can handle or pet the cat. Drying time is dependent upon hair coat length and environmental conditions and may take anywhere from 24–48 hours to dry. It is recommended to wait until product is dry before allowing children to come in contact with a treated cat.