# PARASEDGE™ Multi for Dogs (imidacloprid + moxidectin) Topical Solution

**Once-a-month topical solution for the prevention of heartworm disease, the treatment of circulating microfilariae, kills adult fleas, is indicated for the treatment of flea infestations, the treatment and control of sarcoptic mange, as well as the treatment and control of intestinal parasite infections in dogs and puppies that are at least 7 weeks of age and that weigh at least 3 lbs.**

**WARNING**

- **DO NOT ADMINISTER THIS PRODUCT ORALLY**
- **For the first 30 minutes after application ensure that dogs cannot lick the product from application sites on themselves or other treated animals.**
- **Children should not come in contact with application sites for two (2) hours after application**
  **(See Contraindications, Warnings, Human Warnings, and Adverse Reactions, for more information.)**

**CAUTION:**
Federal (U.S.A.) Law restricts this drug to use by or on the order of a licensed veterinarian.

**DESCRIPTION:**
PARASEDGE™ Multi for Dogs (10 % imidacloprid + 2.5 % moxidectin) is a colorless to yellow ready-to-use solution packaged in single dose applicator tubes for topical treatment of dogs. The formulation and dosage schedule are designed to provide a minimum of 4.5 mg/lb (10 mg/kg) imidacloprid and 1.1 mg/lb (2.5 mg/kg) moxidectin based on body weight.

Imidacloprid is a chloronicotinyl nitroguanidine insecticide. The chemical name for imidacloprid is 1-[(6-Chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine. Moxidectin is a semisynthetic macrocyclic lactone endectocide derived from the actinomycete *Streptomycetes cyaneogriseus noncyanogenus*. The chemical name for moxidectin is [6R, 23E, 25S(E)]-5-O-Demethyl-28-deoxy-25-(1,3-dimethyl-1-butenyl)-6,28-epoxy-23-(methoxyimino) milbemycin B.

**INDICATIONS:**
PARASEDGE™ Multi for Dogs is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and the treatment of *Dirofilaria immitis* circulating microfilariae in heartworm-positive dogs. PARASEDGE™ Multi for Dogs kills adult fleas and is indicated for the treatment of flea infestations *(Ctenocephalides felis)*. PARASEDGE™ Multi for Dogs is indicated for the treatment and control of sarcoptic mange caused by *Sarcoptes scabiei var. canis*. PARASEDGE™ Multi for Dogs is also indicated for the treatment and control of the following intestinal parasites:

| Intestinal Parasite | | Intestinal Stage | | |
|---|---|---|---|---|
| | | Adult | Immature Adult | Fourth Stage Larvae |
| Hookworm Species | *Ancylostoma caninum* | X | X | X |
| | *Uncinaria stenocephala* | X | X | X |
| Roundworm Species | *Toxocara canis* | X | | X |
| | *Toxascaris leonina* | X | | |
| Whipworm | *Trichuris vulpis* | X | | |

**CONTRAINDICATIONS:**
**Do not administer this product orally. (See WARNINGS.)**
**Do not use this product (containing 2.5 % moxidectin) on cats.**

**WARNINGS:**
**For the first 30 minutes after application:**
**Ensure that dogs cannot lick the product from application sites on themselves or other treated dogs.**

**Separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.**

**Ingestion of this product by dogs may cause serious adverse reactions including depression, salivation, dilated pupils, incoordination, panting, and generalized muscle tremors.**

**In avermectin sensitive dogs,[a] the signs may be more severe and may include coma and death.[b]**

[a] Some dogs are more sensitive to avermectins due to a mutation in the MDR1 gene. Dogs with this mutation may develop signs of severe avermectin toxicity if they ingest this product. The most common breeds associated with this mutation include Collies and Collie crosses.

[b] Although there is no specific antagonist for avermectin toxicity, even severely affected dogs have completely recovered from avermectin toxicity with intensive veterinary supportive care.

**HUMAN WARNINGS:**
**Not for human use. Keep out of the reach of children.**
**Children should not come in contact with application sites for two (2) hours after application.**

Causes eye irritation. Harmful if swallowed. Do not get in eyes or on clothing. Avoid contact with skin. Exposure to the product has been reported to cause headache; dizziness; and redness, burning, tingling, or numbness of the skin. **Wash hands thoroughly with soap and warm water after handling.**

If contact with eyes occurs, hold eyelids open and flush with copious amounts of water for 15 minutes. If eye irritation develops or persists, contact a physician. If swallowed, call poison control center or physician 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 the poison control center or physician. People with known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the product with caution. In case of allergic reaction, contact a physician. If contact with skin or clothing occurs, take off contaminated clothing. Wash skin immediately with plenty of soap and water. Call a poison control center or physician for treatment advice.

The safety data sheet (SDS) provides additional occupational safety information. To report suspected adverse drug events, for technical assistance or to obtain a copy of the SDS, contact Virbac AH, Inc. at 1-800-338-3659 or us.virbac.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

**PRECAUTIONS:**
Do not dispense dose applicator tubes without complete safety and administration information.

Use with caution in sick, debilitated, or underweight animals. The safety of PARASEDGE™ Multi for Dogs has not been established in breeding, pregnant, or lactating dogs. The safe use of PARASEDGE™ Multi for Dogs has not been established in puppies and dogs less than 7 weeks of age or less than 3 lbs. body weight.

Prior to administration of PARASEDGE™ Multi for Dogs, dogs should be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to remove adult heartworms. The safety of PARASEDGE™ Multi for Dogs has not been evaluated when administered on the same day as an adulticide. PARASEDGE™ Multi for Dogs is not effective against adult *D. immitis*. Although the number of circulating microfilariae is substantially reduced in most dogs following treatment with PARASEDGE™ Multi for Dogs, the microfilaria count in some heartworm-positive dogs may increase or remain unchanged following treatment with PARASEDGE™ Multi for Dogs alone or in a dosing regimen with melarsomine dihydrochloride. **(See ADVERSE REACTIONS and ANIMAL SAFETY - Safety Study in Heartworm-Positive Dogs.)**

PARASEDGE™ Multi for Dogs has not been evaluated in heartworm-positive dogs with Class 4 heartworm disease.

**ADVERSE REACTIONS:**

**Heartworm-Negative Dogs**

**Field Studies:** Following treatment with imidacloprid and moxidectin topical solution or an active control, dog owners reported the following post-treatment reactions:

| OBSERVATION | imidacloprid and moxidectin topical solution n=128 | Active Control n=68 |
|---|---|---|
| Pruritus | 19 dogs (14.8 %) | 7 dogs (10.3 %) |
| Residue | 9 dogs (7.0 %) | 5 dogs (7.4 %) |
| Medicinal Odor | 5 dogs (3.9 %) | None observed |
| Lethargy | 1 dog (0.8 %) | 1 dog (1.5 %) |
| Inappetence | 1 dog (0.8 %) | 1 dog (1.5 %) |
| Hyperactivity | 1 dog (0.8 %) | None observed |

During a field study using 61 dogs with pre-existing flea allergy dermatitis, one (1.6 %) dog experienced localized pruritus immediately after imidacloprid application, and one investigator noted hyperkeratosis at the application site of one dog (1.6 %).

In a field safety and effectiveness study, imidacloprid and moxidectin topical solution was administered to 92 client-owned dogs with sarcoptic mange. The dogs ranged in age from 2 months to 12.5 years and ranged in weight from 3 to 231.5 pounds. Adverse reactions in dogs treated with imidacloprid and moxidectin topical solution included hematochezia, diarrhea, vomiting, lethargy, inappetence, and pyoderma.

**Laboratory Effectiveness Studies:** One dog in a laboratory effectiveness study experienced weakness, depression, and unsteadiness between 6 and 9 days after application with imidacloprid and moxidectin topical solution. The signs resolved without intervention by day 10 post-application. The signs in this dog may have been related to peak serum levels of moxidectin, which vary between dogs, and occur between 1 and 21 days after application of imidacloprid and moxidectin topical solution.

The following clinical observations also occurred in laboratory effectiveness studies following application with imidacloprid and moxidectin topical solution and may be directly attributed to the drug or may be secondary to the intestinal parasite burden or other underlying conditions in the dogs: diarrhea, bloody stools, vomiting, anorexia, lethargy, coughing, ocular discharge and nasal discharge. Observations at the application sites included damp, stiff or greasy hair, the appearance of a white deposit on the hair, and mild erythema, which resolved without treatment within 2 to 48 hours.

**Heartworm-Positive Dogs**

**Field Study:** A 56-day field safety study was conducted in 214 *D. immitis* heartworm and microfilaria positive dogs with Class 1, 2 or 3 heartworm disease. All dogs received imidacloprid and moxidectin topical solution on Study Days 0 and 28; 108 dogs also received melarsomine dihydrochloride on Study Days -14, 14 and 15. All dogs were hospitalized for a minimum of 12 hours following each treatment. Effectiveness against circulating *D. immitis* microfilariae was > 90 % at five of six sites; however, one site had an effectiveness of 73.3 %. The microfilaria count in some heartworm-positive dogs increased or remained unchanged following treatment with imidacloprid and moxidectin topical solution alone or in a dosing regimen with melarsomine dihydrochloride.

Following treatment with imidacloprid and moxidectin topical solution alone or in a dosing regimen with melarsomine dihydrochloride, the following adverse reactions were observed:

| Adverse Reaction | Dogs Treated with imidacloprid and moxidectin topical solution Only n=106 | Dogs Treated with imidacloprid and moxidectin topical solution + Melarsomine n=108 |
|---|---|---|
| Cough | 24 (22.6 %) | 25 (23.1 %) |
| Lethargy | 14 (13.2 %) | 42 (38.9 %) |
| Vomiting | 11 (10.4 %) | 18 (16.7 %) |
| Diarrhea, including hemorrhagic | 10 (9.4 %) | 22 (20.4 %) |
| Inappetence | 7 (6.6 %) | 19 (17.6 %) |
| Dyspnea | 6 (5.7 %) | 10 (9.3 %) |
| Tachypnea | 1 (< 1 %) | 7 (6.5 %) |
| Pulmonary Hemorrhage | 0 | 1 (< 1 %) |
| Death | 0 | 3 (2.8 %) |

Three dogs treated with imidacloprid and moxidectin topical solution in a dosing regimen with melarsomine dihydrochloride died of pulmonary embolism from dead and dying heartworms. One dog, treated with imidacloprid and moxidectin topical solution and melarsomine dihydrochloride, experienced pulmonary hemorrhage and responded to supportive medical treatment. Following the first treatment with imidacloprid and moxidectin topical solution alone, two dogs experienced adverse reactions (coughing, vomiting, and dyspnea) that required hospitalization. In both groups, there were more adverse reactions to imidacloprid and moxidectin topical solution following the first treatment than the second treatment.

To report a suspected adverse reaction, call 1-800-338-3659.

**Post-Approval Experience**

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using this data. The following adverse events in dogs are listed in decreasing order of reporting frequency: depression/lethargy, vomiting, pruritus, diarrhea, anorexia, hyperactivity, ataxia, trembling, hypersalivation, application site reactions (alopecia, pruritus, lesions, and erythema), seizures, and anaphylaxis/anaphylactic reactions (hives, urticaria, facial swelling, edema of the head).

**Serious reactions, including neurologic signs and death have been reported when cats have been exposed (orally and topically) to this product.**

In humans, nausea, numbness or tingling of the mouth/lips and throat, ocular and dermal irritation, pruritus, headache, vomiting, diarrhea, depression and dyspnea have been reported following exposure to this product.

To report suspected adverse events and/or obtain a copy of the SDS or for technical assistance, call VIRBAC AH, Inc. at 1-800-338-3659.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/reportanimalae.

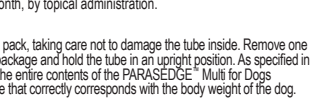
**DOSAGE AND ADMINISTRATION:**
The recommended minimum dose is 4.5 mg/lb (10 mg/kg) imidacloprid and 1.1 mg/lb (2.5 mg/kg) moxidectin, once a month, by topical administration.

Do not apply to irritated skin.

**1.** Use scissors to open the foil pack, taking care not to damage the tube inside. Remove one dose applicator tube from the package and hold the tube in an upright position. As specified in the following table, administer the entire contents of the PARASEDGE™ Multi for Dogs (imidacloprid + moxidectin) tube that correctly corresponds with the body weight of the dog.

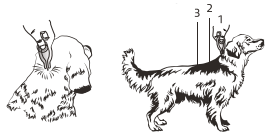
| Dog (lbs.) | PARASEDGE™ Multi for Dogs | Volume (mL) | Imidacloprid (mg) | Moxidectin (mg) |
|---|---|---|---|---|
| 3 - 9 | PARASEDGE™ Multi 9 | 0.4 | 40 | 10 |
| 9.1 - 20 | PARASEDGE™ Multi 20 | 1.0 | 100 | 25 |
| 20.1 - 55 | PARASEDGE™ Multi 55 | 2.5 | 250 | 62.5 |
| 55.1 - 88 | PARASEDGE™ Multi 88 | 4.0 | 400 | 100 |
| 88.1 - 110* | PARASEDGE™ Multi 110 | 5.0 | 500 | 125 |

*Dogs over 110 lbs. should be treated with the appropriate combination of PARASEDGE™ Multi for Dogs tubes.




**2.** Bend the tip back until it snaps off. If it doesn't snap off at first, cut it using scissors.

**3.** The dog should be standing for application. Part the hair on the back of the dog between the shoulder blades until the skin is visible. For dogs weighing 20 lbs. or less, place the tip of the tube on the skin and apply the entire contents directly on the exposed skin at one spot between the shoulder blades. For dogs weighing more than 20 lbs., place the tip of the tube on the skin and apply the entire contents directly on the exposed skin at 3 or 4 spots on the top of the backline from the base of the neck to the upper back in an area inaccessible to licking. Do not apply an amount of solution at any one location that could run off the side of the dog.




**4.** Keep tube compressed on the final squeeze to avoid drawing liquid back into tube. While keeping tube squeezed, drag it away from liquid and lift up to remove.

**5.** Ensure tube is empty.

Do not let this product get in your dog's mouth or eyes. **Do not allow the dog to lick any of the application sites for 30 minutes.** In households with multiple pets, keep each treated dog separated from other treated dogs and other pets for 30 minutes after application to prevent licking the application sites. **(See WARNINGS.)**

Stiff hair, a damp appearance of the hair, pink skin, or a slight powdery residue may be observed at the application site on some animals. This is temporary and does not affect the safety and effectiveness of the product.

Shampooing 90 minutes after treatment does not reduce the effectiveness of PARASEDGE™ Multi for Dogs in the prevention of heartworm disease. Shampooing or water immersion 4 days after treatment will not reduce the effectiveness of PARASEDGE™ Multi for Dogs in the treatment of flea infestations. However, shampooing as often as once weekly may reduce the effectiveness of the product against fleas.

**Heartworm Prevention:** For prevention of heartworm disease, PARASEDGE™ Multi for Dogs should be administered at one-month intervals. PARASEDGE™ Multi for Dogs may be administered year-round or at a minimum should start one month before the first expected exposure to mosquitoes and should continue at monthly intervals until one month after the last exposure to mosquitoes. If a dose is missed and a 30-day interval between doses is exceeded, administer PARASEDGE™ Multi for Dogs immediately and resume the monthly dosing schedule. When replacing another heartworm preventative product in a heartworm prevention program, the first treatment with PARASEDGE™ Multi for Dogs should be given within one month of the last dose of the former medication.

**Treatment of Circulating Microfilaria:** For the treatment of circulating *D. immitis* microfilaria in heartworm-positive dogs, PARASEDGE™ Multi for Dogs should be administered at one-month intervals. Treatment with an approved adulticide therapy is recommended because PARASEDGE™ Multi for Dogs is not effective for the treatment of adult *D. immitis*. **(See PRECAUTIONS.)**

**Flea Treatment:** For the treatment of flea infestations, PARASEDGE™ Multi for Dogs should be administered at one-month intervals. If the dog is already infested with fleas when the first dose of PARASEDGE™ Multi for Dogs is administered, adult fleas on the dog will be killed. However, reinfestation from the emergence of pre-existing pupae in the environment may continue to occur for six weeks or longer after treatment is initiated. Dogs treated with imidacloprid, including those with pre-existing flea allergy dermatitis have shown clinical improvement as a direct result of elimination of fleas from the dog.

**Treatment and Control of Intestinal Nematode Infections:**
For the treatment and control of intestinal hookworm infections caused by *Ancylostoma caninum* and *Uncinaria stenocephala* (adults, immature adults and fourth stage larvae) and roundworm infections caused by *Toxocara canis* (adults and fourth stage larvae), and *Toxascaris leonina* (adults), and whipworm infections caused by *Trichuris vulpis* (adults), PARASEDGE™ Multi for Dogs should be administered once as a single topical dose.

**Treatment and Control of Sarcoptic Mange:** For the treatment and control of sarcoptic mange caused by *Sarcoptes scabiei var. canis*, PARASEDGE™ Multi for Dogs should be administered as a single topical dose. A second monthly dose may be administered if necessary.

**ANIMAL SAFETY:**

**Heartworm-Negative Dogs**

**Field Study:** In a controlled, double-masked, field safety study, imidacloprid and moxidectin topical solution was administered to 128 dogs of various breeds, 3 months to 15 years of age, weighing 4 to 157 pounds. Imidacloprid and moxidectin topical solution was used safely in dogs concomitantly receiving ACE inhibitors, anticonvulsants, antihistamines, antimicrobials, chondroprotectants, corticosteroids, immunotherapeutics, MAO inhibitors, NSAIDs, ophthalmic medications, sympathomimetics, synthetic estrogens, thyroid hormones, and urinary acidifiers. Owners reported the following signs in their dogs after application of imidacloprid and moxidectin topical solution: pruritus, flaky/greasy residue at the treatment site, medicinal odor, lethargy, inappetence, and hyperactivity. **(See ADVERSE REACTIONS.)**

**Safety Study in Puppies:** Imidacloprid and moxidectin topical solution was applied topically at 1, 3 and 5X the recommended dose to 7-week-old Beagle puppies once every 2 weeks for 6 treatments on days 0, 14, 28, 42, 56 and 70. Loose stools and diarrhea were observed in all groups, including the controls, throughout the study. Vomiting was seen in one puppy from the 1X treatment group (day 57), in two puppies from the 3X treatment group (days 1 and 79), and in one puppy from the 5X treatment group (day 1). Two puppies each in the 1X, 3X, and 5X groups had decreased appetites within 24 hours post-dosing. One puppy in the 1X treatment group had pruritus for one hour following the fifth treatment. A puppy from the 5X treatment group displayed rapid, difficult breathing from 4 to 8 hours following the second treatment.

**Dermal Dose Tolerance Study:** Imidacloprid and moxidectin topical solution was administered topically to 8-month-old Beagle dogs at 10X the recommended dose once. One dog showed signs of treatment site irritation after application. Two dogs vomited, one at 6 hours and one at 6 days post-treatment. Increased RBC, hemoglobin, activated partial thromboplastin, and direct bilirubin were observed in the treated group. Dogs in the treated group did not gain as much weight as the control group.

**Oral Safety Study in Beagles:** Imidacloprid and moxidectin topical solution was administered once orally at the recommended topical dose to 12 dogs. Six dogs vomited within 1 hour of receiving the test article, 2 of these dogs vomited again at 2 hours, and 1 dog vomited again up to 18 hours post-dosing. One dog exhibited shaking (nervousness) 1 hour post-dosing. Another dog exhibited abnormal neurological signs (circling, ataxia, generalized muscle tremors, and dilated pupils with a slow pupillary light response) starting at 4 hours post-dosing through 18 hours post-dosing. Without treatment, this dog was neurologically normal at 24 hours and had a normal appetite by 48 hours post-dosing. **(See CONTRAINDICATIONS.)**

**Dermal Safety Study in Ivermectin-Sensitive Collies:**
Imidacloprid and moxidectin topical solution was administered topically at 3 and 5X the recommended dose every 28 days for 3 treatments to Collies which had been pre-screened for avermectin sensitivity. No clinical abnormalities were observed.

**Oral Safety Study in Ivermectin-Sensitive Collies:**
Imidacloprid and moxidectin topical solution was administered orally to 5 pre-screened ivermectin-sensitive Collies. The Collies were asymptomatic after ingesting 10 % of the minimum labeled dose. At 40 % of the minimum recommended topical dose, 4 of the dogs experienced neurological signs indicative of avermectin toxicity including depression, ataxia, mydriasis, salivation, muscle fasciculation, and coma, and were euthanized. **(See CONTRAINDICATIONS.)**

**Heartworm-Positive Dogs**

**Laboratory Safety Study in Heartworm-Positive Dogs:** Imidacloprid and moxidectin topical solution was administered topically at 1 and 5X the recommended dose every 14 days for 3 treatments to dogs with adult heartworm infections and circulating microfilaria. At 5X, one dog was observed vomiting three hours after the second treatment. Hypersensitivity reactions were not seen in the 5X treatment group. Microfilaria counts decreased with treatment.

**STORAGE INFORMATION:** Store below 25°C (77°F).

**HOW SUPPLIED:**
Applications Per Package : 3 x 0.4 mL tubes, 3 x 1.0 mL tubes, 3 x 2.5 mL tubes, 3 x 4.0 mL tubes, 3 x 5.0 mL tubes

Approved by FDA under ANADA # 200-700

PARASEDGE™ is a trademark of Virbac S.A.


Manufactured for: Virbac AH, Inc., P.O. Box 162059, Fort Worth, TX 76161

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