IMOXI™ Topical Solution for Dogs
(imidacloprid + moxidectin)

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 (USA) Law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
IMOXI™ Topical Solution 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-dimethl-1-butenyl)-6,28-epoxy-23-(methoxyimino) milbemycin B.

INDICATIONS:
IMOXI™ Topical Solution 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. IMOXI™ Topical Solution for Dogs kills adult fleas and is indicated for the treatment of flea infestations (*Ctenocephalides felis*). IMOXI™ Topical Solution for Dogs is indicated for the treatment and control of sarcoptic mange caused by *Sarcoptes scabiei* var. *canis*. IMOXI™ Topical Solution 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, and 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. For consumer questions call 1-800-835-9496.

For a copy of the Safety Data Sheet (SDS) or to report adverse reactions call Vetoquinol USA, Inc. at 1-800-835-9496.

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 IMOXI™ Topical Solution for Dogs has not been established in breeding, pregnant, or lactating dogs. The safe use of IMOXI™ Topical Solution 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 IMOXI™ Topical Solution 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 IMOXI™ Topical Solution for Dogs has not been evaluated when administered on the same day as an adulticide. IMOXI™ Topical Solution for Dogs is not effective against adult *D. immitis*. Although the number of circulating microfilariae is substantially reduced in most dogs following treatment with IMOXI™ Topical Solution for Dogs, the microfilaria count in some heartworm-positive dogs may increase or remain unchanged following treatment with IMOXI™ Topical Solution for Dogs, alone or in a dosing regimen with melarsomine dihydrochloride.

(See ADVERSE REACTIONS and ANIMAL SAFETY – Safety Study in Heartworm-Positive Dogs.)
IMOXI™ Topical Solution 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 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 1-800-835-9496.

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 drug events, for technical assistance or to obtain a copy of the SDS, contact Vetoquinol USA, Inc. at 1-800-835-9496.

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.

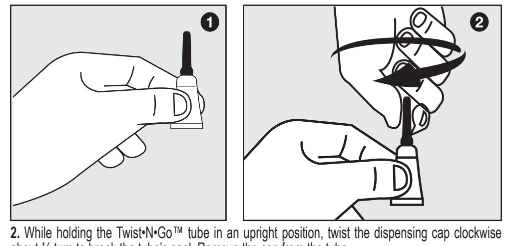
DOSAGE AND ADMINISTRATION:
The recommended minimum dose is 4.5 mg/lb. (10 mg/kg) imidacloprid and 1.1 mg/lb. (2.5 mg/kg) moxidectin, once a month, by topical administration.

Do not apply to irritated skin.

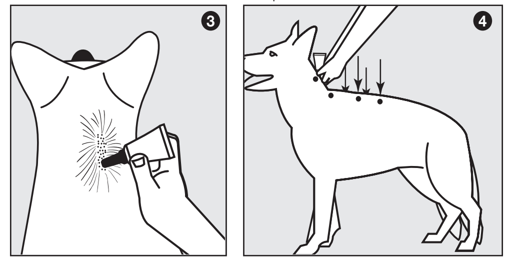
1. Remove one dose applicator tube from the package. As specified in the table, administer the entire contents of the IMOXI™ Topical Solution for Dogs tube that correctly corresponds with the body weight of the dog.

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

* Dogs over 110 lbs. should be treated with the appropriate combination of IMOXI™ Topical Solution for Dogs tubes.



2. While holding the Twist•N•Go™ tube in an upright position, twist the dispensing cap clockwise about ½ turn to break the tube's seal. Remove the cap from the tube.



3. The dog should be standing for application. Position the dispensing tip on the dog's back between the shoulder blades. The dispensing tip of the tube can be used to part the dog's hair until the skin is visible.

4. 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.

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 IMOXI™ Topical Solution for Dogs in the prevention of heartworm disease. Shampooing or water immersion 4 days after treatment will not reduce the effectiveness of IMOXI™ Topical Solution 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, IMOXI™ Topical Solution for Dogs should be administered at one-month intervals. IMOXI™ Topical Solution 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 IMOXI™ Topical Solution for Dogs immediately and resume the monthly dosing schedule. When replacing another heartworm preventative product in a heartworm prevention program, the first treatment with IMOXI™ Topical Solution 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, IMOXI™ Topical Solution for Dogs should be administered at one-month intervals. Treatment with an approved adulticide therapy is recommended because IMOXI™ Topical Solution for Dogs is not effective for the treatment of adult *D. immitis*.
(See PRECAUTIONS)

Flea Treatment: For the treatment of flea infestations, IMOXI™ Topical Solution for Dogs should be administered at one-month intervals. If the dog is already infested with fleas when the first dose of IMOXI™ Topical Solution for Dogs is administered, adult fleas on the dog will be killed. However, reinfestation from the emergence of preexisting 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), IMOXI™ Topical Solution 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*, IMOXI™ Topical Solution 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, imrnunotherapeutics, 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 I0X 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 prescreened 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 at temperatures between 20° C (68 °F) and 25° C (77 °F), avoiding excess heat or cold.

HOW SUPPLIED:

Applications Per Package:		
	6 x 0.4 mL tubes	6 x 4.0 mL tubes
	6 x 1.0 mL tubes	6 x 5.0 mL tubes
	6 x 2.5 mL tubes	

vetoquinol

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Approved by FDA under ANADA # 200-615
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IMOXI™ Topical Solution for Cats
(imidacloprid + moxidectin)

Once-a-month topical solution for cats for the prevention of heartworm disease, kills adult fleas, is indicated for the treatment of flea infestations, as well as the treatment and control of ear mite infestations and intestinal parasite infections in cats and kittens 9 weeks of age and older and that weigh at least 2 lbs.

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

DESCRIPTION:
IMOXI™ Topical Solution for Cats (10% imidacloprid + 1% moxidectin) is a colorless to yellow ready-to-use solution packaged in single-dose applicator tubes for topical treatment of cats. The formulation and dosage schedule are designed to provide a minimum of 4.5 mg/lb (10.0 mg/kg) imidacloprid and 0.45 mg/lb (1.0 mg/kg) moxidectin based on body weight.

Imidacloprid is a chloronicotinyl nitroguanidine insecticide. The chemical name of 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 of 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:
IMOXI™ Topical Solution for Cats is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*. IMOXI™ Topical Solution for Cats kills adult fleas *(Ctenocephalides felis)* and is indicated for the treatment of flea infestations. IMOXI™ Topical Solution for Cats is also indicated for the treatment and control of ear mite *(Otodectes cynotis)* infestations and the following intestinal parasites:

Intestinal Parasite		Intestinal Stage		
		Adult	Immature Adult	Fourth Stage Larvae
Hookworm Species	*Ancylostoma tubaeforme*	X	X	X
Roundworm Species	*Toxocara cati*	X		X

WARNINGS:
Do not use on sick, debilitated, or underweight cats (see ADVERSE REACTIONS). Do not use on cats less than 9 weeks of age or less than 2 lbs. body weight.

HUMAN WARNINGS:
Not for human use. Keep out of the reach of children.
Children should not come in contact with the application site for 30 minutes 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 Vetoquinol USA at 1-800-835-9496 or www.vetoquinolusa.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.

Avoid oral ingestion. Cats may experience hypersalivation, tremors, vomiting and decreased appetite if IMOXI™ Topical Solution for Cats is inadvertently administered orally or through grooming/licking of the application site.

The safety of IMOXI™ Topical Solution for Cats has not been established in breeding, pregnant, or lactating cats.

The effectiveness of IMOXI™ Topical Solution for Cats against heartworm infections *(D. immitis)* after bathing has not been evaluated in cats.

Use of this product in geriatric patients with subclinical conditions has not been adequately studied. Several otherwise healthy, thin geriatric cats experienced prolonged lethargy and sleepiness after using imidacloprid and moxidectin topical solution. **(See ADVERSE REACTIONS).**

ADVERSE REACTIONS:
Field Study: Following treatment with imidacloprid and moxidectin topical solution or an active control, cat owners reported the following post-treatment reactions:

OBSERVATION	Imidacloprid and Moxidectin Topical Solution n=113	Active Control n=38
Lethargy (protracted sleeping, poorly responsive)	3 cats* (2.7%)	None observed
Behavioral changes (e.g., agitated, excessive grooming, hiding, pacing, spinning)	9 cats (8.0%)	1 cat (2.6%)
Discomfort (e.g., scratching, rubbing, head-shaking)	5 cats (4.4%)	None observed
Hypersalivation (within 1 hour after treatment)	3 cats (2.7%)	None observed
Polydipsia	3 cats (2.7%)	None observed
Coughing and gagging	1 cat (0.9%)	None observed

* These three cats were from the same household and included one 13-yr-old cat in good health, one 15-yr-old FIV positive cat in good health, and one 15-yr-old, underweight cat in fair health. Lethargy was noted for 24 to 36 hrs after the first treatment only; one cat was unsteady at 48hrs. These cats were not on other medications.

During another field study, a 16-year-old cat with renal disease slept in the same place without moving for two days following application.
(See PRECAUTIONS).

Laboratory Effectiveness Studies: Imidacloprid and moxidectin topical solution was administered at the recommended dose to 215 cats in 20 effectiveness studies. One random-sourced cat exhibited signs consistent with either moxidectin toxicity or viral respiratory disease and died 26 hours after product application; necropsy findings were inconclusive as to the cause of death. A second cat that became ill 3 days after application of imidacloprid and moxidectin topical solution responded to treatment for respiratory infection and completed the study. A third cat became ill on day 3 and died with signs and lesions attributable to panleukopenia on day 7 after moxidectin application.

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 cats are listed in decreasing order of reporting frequency: hypersalivation, depression/lethargy, application site reactions (alopecia, pruritus, lesions, and erythema), decreased appetite, vomiting, hyperactivity, ataxia, trembling, and behavior disorder (hiding).

In some cases, death has been reported.

In humans, ocular and dermal irritation, nausea, numbness or tingling of the mouth and lips, anaphylaxis, pruritus, vomiting, and tongue/taste abnormalities have been reported following exposure to imidacloprid and moxidectin topical solution.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the SDS, contact Vetoquinol USA at 1-800-835- 9496 or www.vetoquinolusa.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.

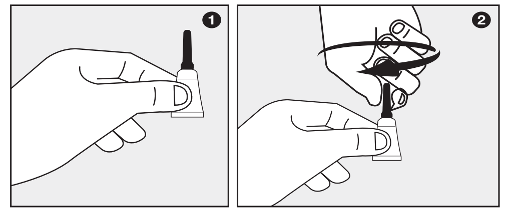
DOSAGE AND ADMINISTRATION:
The recommended minimum dose is 4.5 mg/lb (10.0 mg/kg) imidacloprid and 0.45 mg/lb (1.0 mg/kg) moxidectin, once a month, by topical administration.

Do not apply to irritated skin.

1. Remove one dose applicator tube from the package. As specified in the following table, administer the entire contents of the IMOXI™ Topical Solution for Cats tube that correctly corresponds with the body weight of the cat.

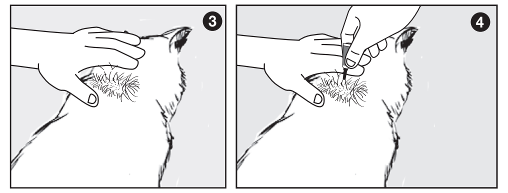
Cat (lbs.)	Volume (mL)	Imidacloprid (mg)	Moxidectin (mg)
2-5	0.23	23	2.3
5.1-9	0.4	40	4
9.1-18*	0.8	80	8

* Cats over 18 lbs. should be treated with the appropriate combination of IMOXI™ Topical Solution for Cats tubes.



2. While holding the Twist•N•Go™ tube in an upright position, twist dispensing tip clockwise about ½ turn to break the tube's seal. Remove the cap from the tube.

3. Part the hair on the back of the cat's neck at the base of the head, until the skin is visible.



4. Place the tip of the tube on the skin and apply the entire contents directly on the exposed skin. Lift the tube away from the skin before releasing pressure on the tube.

Do not get this product in the cat's mouth or eyes or allow the cat to lick the application site for 30 minutes. Treatment at the base of the head will minimize the opportunity for ingestion by grooming. In households with multiple pets, keep animals separated to prevent licking of the application site.

Stiff, matted hair or a damp, oily appearance of the hair may be observed at the application site on some cats. This is temporary and does not affect the safety and effectiveness of the product.

Heartworm Prevention: For prevention of heartworm disease, IMOXI™ Topical Solution for Cats should be administered at one-month intervals. IMOXI™ Topical Solution for Cats may be administered year-around 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 IMOXI™ Topical Solution for Cats immediately and resume the monthly dosing schedule. When replacing another heartworm preventative product in a heartworm prevention program, the first treatment with IMOXI™ Topical Solution for Cats should be given within one month of the last dose of the former medication. At the discretion of the veterinarian, cats older than 6 months of age may be tested to determine the presence of existing heartworm infection before treatment with IMOXI™ Topical Solution for Cats. **(See ADVERSE REACTIONS – Post-Approval Experience).**

Flea Treatment: For the treatment of flea infestations, IMOXI™ Topical Solution for Cats should be administered at one-month intervals. If the cat is already infested with fleas when the first dose of IMOXI™ Topical Solution for Cats is administered, adult fleas on the cat will be killed. However, re-infestation from the emergence of pre-existing pupae in the environment may continue to occur for six weeks or longer after treatment is initiated. Cats 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 cat.

Ear Mite Treatment: For the treatment of ear mites (*Otodectes cynotis*), IMOXI™ Topical Solution for Cats should be administered once as a single topical dose. Monthly use of IMOXI™ Topical Solution for Cats will control any subsequent ear mite infestations.

Intestinal Nematode Treatment: For the treatment and control of intestinal hookworm infections caused by *Ancylostoma tubaeforme* (adults, immature adults and fourth stage larvae) and roundworm infections caused by *Toxocara cati* (adults and fourth stage larvae), IMOXI™ Topical Solution for Cats should be administered once as a single topical dose.

ANIMAL SAFETY:
Studies in Kittens: Imidacloprid and moxidectin topical solution was topically applied at 0, 1, 3, and 5X the maximum dose to 48 healthy 9-week-old kittens on days 0, 28, and 56. Lethargy was observed in 1 kitten from the 3X group and 1 from the 5X group on the day after initial treatment; the kitten from the 3X group was also disoriented and ataxic. One kitten from the 3X group had a slow pupillary light response two days after treatment and one had tremors the day after treatment. Hypersalivation was seen in one kitten from the 5X group approximately six hours post-treatment. One kitten from the 3X group was scratching at the treatment site 2 days after treatment. Slight cough was noted in 7 different kittens (2-0X, 2-1X, and 3-5X) during the 13-day period following the first treatment. Histopathology showed granulomatous inflammation at the treatment site in three 1X kittens. Causal relationship to the drug could not be determined. Pulmonary inflammation (1-5X) and lymphoid hyperplasia (2-1X, 4-3X) were seen in treated kittens. In a second study, imidacloprid and moxidectin topical solution was topically applied at 0, 1.7, 5.2 and 8.7X the maximum dose to 48 healthy 9-week-old kittens every two weeks for 6 doses. One kitten in the 8.7X group apparently ingested an unknown amount of the drug and developed the following clinical signs prior to euthanasia: mydriasis, salivation, depression, vomiting, unsteadiness, rapid to slow to difficult breathing, poor pupillary response, generalized tremors, inability to move, and nystagmus. Two kittens in the 5.2X group developed mydriasis, salivation, depression, squinting, and poor appetite. A kitten in the 1.7X group developed mydriasis.

Dose Tolerance Study: Eight healthy juvenile cats were topically dosed with a single application of imidacloprid and moxidectin topical solution at 10 times the recommended dose volume. Mild, transient hypersalivation occurred in two of the cats.

Oral Study in Cats: The oral safety of imidacloprid and moxidectin topical solution was tested in case of accidental oral ingestion. The maximum topical dose was orally administered to twelve healthy 9-week-old kittens. Hypersalivation (8 of 12 kittens) and vomiting (12 of 12 kittens) were observed immediately post-treatment. Tremors developed in one kitten within 1 hour, resolving without treatment within the next hour. All 12 kittens were either anorexic or had decreased appetite for at least 1 day following treatment. In 3 kittens, the anorexia or decreased appetite continued into the second week following treatment. There was a post-treatment loss of body weight in treated kittens compared to control kittens. In a pilot safety study using kittens younger in age and lighter in weight than allowed by product labeling, an 8-week-old kitten weighing 0.6 kg orally received 2X of the label topical dose (0.46 mL/kg). Immediately after dosing, it vomited, had labored breathing and slight tremors. Within 4 hours, it was normal, but was found dead on day 6. Necropsy could not determine the cause of death.

Study in Heartworm Positive Cats: Young adult cats were inoculated subcutaneously with third-stage *D. immitis* larvae. At 243-245 days post-infection, immunoserology and echocardiography were performed to identify cats with adult heartworm burdens similar to naturally-acquired infections. Two groups were treated topically with either imidacloprid and moxidectin topical solution at the label dose or placebo, once every 28 days, for three consecutive treatments. A third group was treated topically, once, with imidacloprid and moxidectin topical solution at 5X the label dose. Sporadic vomiting and labored breathing related to heartworm burden were observed in the treatment and control groups. There was no difference between treatment groups in the numbers of adult *D. immitis* recovered at study conclusion. No adverse reactions were associated with the topical application of imidacloprid and moxidectin topical solution to experimentally heartworm-infected cats.

STORAGE INFORMATION:
Store at temperatures between 20ºC (68°F) and 25ºC (77°F), avoiding excess heat or cold.

HOW SUPPLIED:
Applications Per Package
3 x 0.23 mL tubes
6 x 0.4 mL tubes
6 x 0.8 mL tubes

Approved by FDA under ANADA # 200-638

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vetoquinol

Vetoquinol USA, Inc.
4250 N. Sylvania Avenue
Ft. Worth, TX 76137

THE PROTECTION PETS NEED AGAINST
BROAD-SPECTRUM EXCUSES

IMOXI™
Topical Solution
(imidacloprid + moxidectin)

Fleas · Heartworms · Intestinal Parasites

CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian. Dogs: 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 the application sites for two (2) hours after application. (See Contraindications, Warnings, Human Warnings and Adverse Reactions for more information.) Cats: Do not use on sick, debilitated, or underweight cats. Avoid oral ingestion. For full prescribing information, see back of document.

vetoquinol
ACHIEVE MORE TOGETHER

All pets need year-round protection against common parasites[1], yet one-third of pets never get the protection they need[2]. New generic Imoxi, a once-a-month topical solution, helps prevent ***fleas, heartworms,*** and ***intestinal parasites*** while making it more affordable for pet owners. The result: ***fewer excuses*** from owners and ***more pets protected.***

IMOXI™
Topical Solution
(imidacloprid + moxidectin)

Proven reliability against a broad spectrum of parasites

Topical moxidectin has been used for decades in dogs and cats and is now available as a generic. Consider using new generic Imoxi for proven protection.

Heartworms
Fleas
Intestinal Parasites

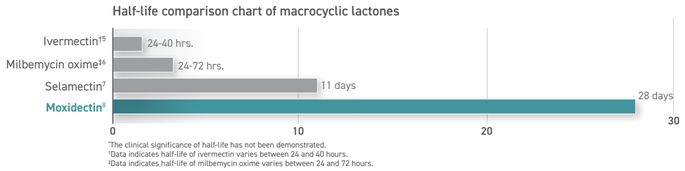
	Dogs and puppies 7 weeks and at least 3 lbs.	Cats and kittens 9 weeks and at least 2 lbs.
Prevents heartworm disease	✓	✓
Treats circulating microfilariae	✓	
Kills adult fleas + treats flea infestations	✓	✓
Treats + controls intestinal parasite infections • Roundworms • Hookworms • Whipworms	✓ ✓ ✓	✓ ✓
Treats + controls sarcoptic mange	✓	
Treats + controls ear mite infestations		✓

Transdermal moxidectin has a unique pharmacologic profile that provides benefits other formulations do not

- It is the only macrocyclic lactone formulation to be FDA-approved as safe and effective for dogs with circulating microfilariae.[3]
- Moxidectin is the only macrocyclic lactone shown to protect against heartworms all month long in dogs.[4]

Moxidectin, the active ingredient in Imoxi, has an extended half-life*

Following transdermal absorption, moxidectin concentrates in the fatty tissue, slowly releasing into the bloodstream, resulting in a long half-life.



[†]The clinical significance of half-life has not been demonstrated.
[‡]Data indicates half-life of ivermectin varies between 24 and 40 hours.
[§]Data indicates half-life of milbemycin oxime varies between 24 and 72 hours.

Imoxi offers unique benefits to your clients, your patients, and your practice.

For your clients:

- ✓ Topical application combining excellent flea, heartworm, and intestinal parasite coverage
- ✓ Twist-N-Go™ cap eliminates a step in the application process

For your patients:

- ✓ Kills fleas through contact — no bite necessary
- ✓ Topical moxidectin is the only formulation approved as a microfilaricide
- ✓ Excellent option for dogs and cats facing reinfection from intestinal parasites due to a contaminated environment
- ✓ Animals with food allergies won't be exposed to oral flavorings

For your practice:

- ✓ Prescription status
- ✓ Lower price allows owners to devote more money toward other pet care services

The Twist-N-Go™ cap eliminates a step in the application process.

Dosing

Dog (lbs.)	Volume (mL)
3-9	0.4
9.1-20	1.0
20.1-55	2.5
55.1-88	4.0
88.1-110*	5.0

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

Cat (lbs.)	Volume (mL)
2-5	0.23
5.1-9	0.4
9.1-18*	0.8

*Cats over 18 lbs. should be treated with the appropriate combination of Imoxi for Cats tubes.

[1]Companion Animal Parasite Council (CAPC). Heartworm Guidelines. Available at: https://capcvet.org/guidelines/heartworm/. [Access date: April 22, 2021]
[2]Pet Product News. Pet Owners Are Alarmingly Unaware About Flea and Tick Dangers, Study Reveals. May 9, 2018. Available at: https://www.petproductnews.com/archives/pet-owners-are-alarmingly-unaware-about-flea-and-tick-dangers-study-reveals/article_014b98cc-75f5-5ed0-b438-1fc4ee65aa86.html. [Access date: April 22, 2021]
[3]Freedom of Information Summary. NADA 141-251 Supplement. Oct. 24, 2013.
[4]Bowman, D.D., Ohmes, C.M., Hostetler, J.A. et al. Efficacy of 10% imidacloprid + 2.5% moxidectin topical solution (Advantage Multi® for Dogs) for the prevention of heartworm disease and infection all month long. Parasites Vectors 10, 478 (2017).
[5]Kojima, K., Yamamoto, K., Katae, H., et al. (1987). Bioavailability of oral ivermectin in dogs. Jpn J Vet Sci. 49(5):899-900.
[6]SENTINEL® Spectrum [Summary of Product Characteristics]. Frimley, Camberley, Surrey, UK: Novartis Animal Health UK Ltd.; May 2008 revision.
[7]Sarasola, P., Jernigan, A.D., Walker, D.K., et al. (2002). Pharmacokinetics of selamectin following intravenous, oral and topical administration in cats and dogs. J Vet Pharmacol Therap. 25(4): 265-272.
[8]Data on file. Bayer, Shawnee Mission, KS.
[9]Veterinary Practice News. Heartworm prevention: Clients can't comply if they don't know that they should. September 5, 2019. Available at: https://www.veterinarypracticenews.com/heartworm-prevention-clients-cant-comply-if-they-dont-know-that-they-should/. [Access date: April 22, 2021].

Good Medicine and Good Business

Imoxi™ (imidacloprid + moxidectin) Topical Solution puts a topical combination you trust within a client's financial reach, which may:

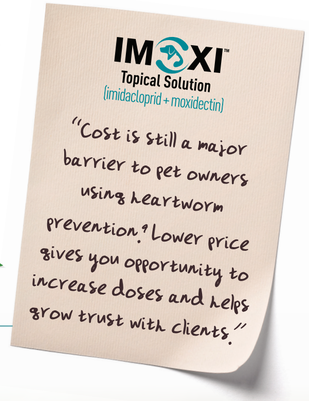
- Help increase the number of doses a pet receives.
- Allow clients to devote more budget to other pet care services.
- Help boost client trust by showing you did the research to find them a way to save.

That's a triple win for your business that offers both short-term revenue and long-term client loyalty.

Support of Vetoquinol

Imoxi is backed by a robust parasite guarantee and by Vetoquinol's Satisfaction Guarantee. Ask your Vetoquinol Territory Manager for details.

SATISFACTION 100% GUARANTEED



To learn more about how Imoxi can help keep more pets protected, contact your Vetoquinol Territory Manager or participating distributor representative or visit imoxitopical.com.

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