

Elanco Paws4Purpose™ Animal Welfare Agreement

Effective: January 1, 2026 - December 31, 2026

PAWS 4 PURPOSE™

TIER 3

\$15K Yearly Commitment | All Brands Eligible

2.5%

Advantage II

Bexacat
(bexagliflozin tablets)

Before using Bexacat, it is important to read the entire package insert including the boxed warning.

Cheristin
for cats
spinetoram

Droncit
(praziquantel)

Drontal
(praziquantel/pyrantel pamoate)

Drontal Plus
(praziquantel/pyrantel pamoate/fenbendazole)

Galliprant
(grapiprant tablets)

K9 Advantix II

profender
(emodepside/praziquantel)

5%

Credelio Quattro
(lotilaner, moxidectin, praziquantel, and pyrantel chewable tablets)

Credelio
(lotilaner)

Credelio CAT (lotilaner)

INTERCEPTOR PLUS
(milbemycin oxime/praziquantel)

onsior
(robenacoxib)

Trifexis
(spinosad+milbemycin oxime)

Zenrelia
(lunocitinib tablets)

Before using Zenrelia, it is important to read the entire package insert including the boxed warning.

7.5%

CLARO
(flufenical, terbinafine, mometasone furoate)
Otic Solution

10%

advantage multi
(imidacloprid+moxidectin)

Seresto

15%

Canine Parvovirus Monoclonal Antibody
CPMA is USDA conditionally approved

30%

Elanco ALL ELANCO VACCINES

truCan

truCan^{ultra}

truFel

truFel^{ultra}

Rabvac

TIER 3+

\$50K Yearly Commitment | Min. \$30K Vaccines and \$20K Para/Thera

5%

Advantage II

Bexacat
(bexagliflozin tablets)

Before using Bexacat, it is important to read the entire package insert including the boxed warning.

Cheristin
for cats
spinetoram

Droncit
(praziquantel)

Drontal
(praziquantel/pyrantel pamoate)

Drontal Plus
(praziquantel/pyrantel pamoate/fenbendazole)

Galliprant
(grapiprant tablets)

K9 Advantix II

profender
(emodepside/praziquantel)

7.5%

Zorbiu
(buprenorphine transdermal solution)

Before using Zorbiu, it is important to read the entire package insert including the boxed human warning.

Credelio Quattro
(lotilaner, moxidectin, praziquantel, and pyrantel chewable tablets)

Credelio
(lotilaner)

Credelio CAT (lotilaner)

INTERCEPTOR PLUS
(milbemycin oxime/praziquantel)

onsior
(robenacoxib)

Trifexis
(spinosad+milbemycin oxime)

10%

CLARO
(flufenical, terbinafine, mometasone furoate)
Otic Solution

12.5%

advantage multi
(imidacloprid+moxidectin)

Zenrelia
(lunocitinib tablets)

onsior
(robenacoxib)

Seresto

Before using Zenrelia, it is important to read the entire package insert including the boxed warning.

20%

Canine Parvovirus Monoclonal Antibody
CPMA is USDA conditionally approved

30%

Elanco ALL ELANCO VACCINES

truCan

truCan^{ultra}

truFel

truFel^{ultra}

Rabvac

BEXACAT INDICATION:

Bexacat is indicated to improve glycemic control in otherwise healthy cats with diabetes mellitus not previously treated with insulin.

BEXACAT IMPORTANT SAFETY INFORMATION:

Before using Bexacat, you must read the entire package insert, including the boxed warning. Call 1-888-545-5973 or visit www.elancolabels.com/us/bexacat for complete safety information.

Cats treated with Bexacat may be at an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis, both of which may result in death. Development of these conditions should be treated promptly, including insulin administration and discontinuation of Bexacat. Do not use Bexacat in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus. The use of Bexacat in cats with insulin-dependent diabetes mellitus, or the withdrawal of insulin and initiation of Bexacat, is associated with an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis and death. Sudden onset of hyporexia/anorexia, lethargy, dehydration, diarrhea that is unresponsive to conventional therapy, or weight loss in cats receiving Bexacat should prompt immediate discontinuation of Bexacat and assessment for diabetic ketoacidosis, regardless of blood glucose level. Bexacat should not be initiated in cats with pancreatitis, anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus, as it may indicate the presence of other concurrent disease and increase the risk of diabetic ketoacidosis. Due to risk of severe adverse reactions, do not use Bexacat in cats with evidence of hepatic disease or reduced renal function. Consult a physician in case of accidental ingestion by humans.

ZENRELIA INDICATIONS:

Zenrelia is indicated for control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

ZENRELIA IMPORTANT SAFETY INFORMATION:

Read the entire package insert, including the Boxed Warning, before using this drug. For full prescribing information call 1 888 545 5973 or visit www.elancolabels.com/us/zenrelia.

WARNING: INADEQUATE IMMUNE RESPONSE TO VACCINES. Based on results of the vaccine response study, dogs receiving Zenrelia are at risk of an inadequate immune response to vaccines. Discontinue Zenrelia for at least 28 days to 3 months prior to vaccination and withhold Zenrelia for at least 28 days after vaccination. Dogs should be up to date on vaccinations prior to starting Zenrelia. Do not use in dogs less than 12 months old or dogs with a serious infection. Monitor dogs for infections because Zenrelia may increase susceptibility to infections, including adenoviral hepatitis and pancreatitis. Neoplastic conditions (benign and malignant) were observed during clinical studies. Consider the risks and benefits of treatment in dogs with a history of recurrence of these conditions. The most common adverse reactions were vomiting, diarrhea and lethargy. Zenrelia has not been evaluated in breeding, pregnant, or lactating dogs and concurrent use with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents has not been tested. For full prescribing information see package insert.

ZORBIUM IMPORTANT SAFETY INFORMATION:

Before using ZORBIUM (buprenorphine transdermal solution), read the entire package insert including the Boxed Human Warning. Call 1-888-545-5973 or visit www.elancolabels.com/us/zorbiu for full prescribing information. ZORBIUM is not for use in humans. ZORBIUM contains buprenorphine, an opioid that exposes humans to risks of misuse, abuse, and addiction, which can lead to overdose and death. Use of buprenorphine may lead to physical dependence. Serious, life-threatening, or fatal respiratory depression may occur with accidental exposure to or with misuse or abuse of ZORBIUM.

Elanco

Elanco Paws4Purpose™ Animal Welfare Agreement

Effective: January 1, 2026 - December 31, 2026



Instructions:

Please complete the form below to finalize your participation in the Elanco Paws4Purpose™ Animal Welfare Agreement for the 2026 program. Ensure all fields are filled out accurately. If any information is missing or incorrect, it may delay the processing of your agreement. Once completed, please submit the form to your Elanco Sales Rep.

Account Name: _____

Elanco Account Number: _____

Required Commitment: \$ _____

Business Phone #: _____

Business Email: _____

Preferred Distributor: _____

Thank you for your commitment to animal welfare and your participation in the Elanco Paws4Purpose™ program. Together, we're making a positive impact on the health and well-being of animals. We appreciate your partnership and dedication!

If a shelter participating in the Paws 4 Purpose program sells Elanco product(s) to an unauthorized reseller (as solely determined by Elanco), such shelter will be immediately removed from the Paws 4 Purpose program and forfeit all associated pricing.

Advantage, Advantage Multi, Bexacat, Cheristin, Claro, Credelio, Credelio Quattro, Droncit, Drontal, Galliprant, Interceptor, K9 Advantix, profender, Rabvac, Seresto, Trifexis, TruCan, TruFel, UltraNasal, Zenrelia, Zorbium, Elanco and the diagonal bar logo are trademarks of Elanco or its affiliates. Other company and product names are trademarks of their respective owners. © 2025 Elanco or its affiliates. PM-US-25-1889(2)



Contact your Midwest Veterinary Supply Representative for more information!
To place your order: **800-643-9378** | www.midwestvetsupply.com



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

DESCRIPTION:

Advantage 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 *Streptomyces 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:

Advantage 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. *Advantage Multi for Dogs* kills adult fleas and is indicated for the treatment of flea infestations (*Ctenocephalides felis*). *Advantage Multi for Dogs* is indicated for the treatment and control of sarcoptic mange caused by *Sarcoptes scabiei* var. *canis*. *Advantage 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	<i>Ancylostoma caninum</i>	X	X	X
	<i>Uncinaria stenocephala</i>	X	X	X
Roundworm Species	<i>Toxocara canis</i>	X		X
	<i>Toxascaris leonina</i>	X		
Whipworm	<i>Trichuris vulpis</i>	X		

DOSAGE AND ADMINISTRATION:

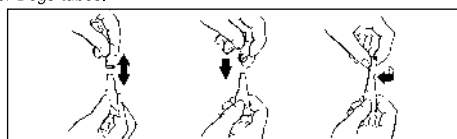
The recommended minimum dose is 4.5 mg/lb (10 mg/kg) imidacloprid and 1.1 mg/lb (2.5 mg/kg) moxidectin, once a month, by topical administration.

Do not apply to irritated skin.

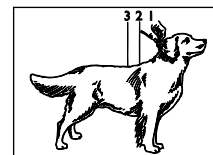
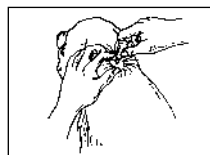
1. Remove one dose applicator tube from the package. As specified in the following table, administer the entire contents of the *Advantage Multi for Dogs* tube that correctly corresponds with the body weight of the dog.

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

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



2. While holding the tube in an upright position, remove the cap from the tube.
3. Turn the cap over and push the other end of cap onto the tip of the tube.
4. Twist the cap to break the seal and then remove cap from the tube.



5. 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.

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**.) Contact with eyes can lead to eye irritation and corneal ulceration. If contact with eyes occurs, hold the dog's eyelids open, flush thoroughly with water, and contact your veterinarian.

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 *Advantage Multi for Dogs* in the prevention of heartworm disease. Shampooing or water immersion 4 days after treatment will not reduce the effectiveness of *Advantage 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, *Advantage Multi for Dogs* should be administered at one-month intervals. *Advantage 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 *Advantage 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 *Advantage 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, *Advantage Multi for Dogs* should be administered at one-month intervals. Treatment with an approved adulticide therapy is recommended because *Advantage Multi for Dogs* is not effective for the treatment of adult *D. immitis*.

(See **PRECAUTIONS**.)

Flea Treatment: For the treatment of flea infestations, *Advantage Multi for Dogs* should be administered at one-month intervals. If the dog is already infested with fleas when the first dose of *Advantage 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), *Advantage 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*, *Advantage Multi for Dogs* should be administered as a single topical dose. A second monthly dose may be administered if necessary.

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 product questions, to report adverse reactions, or for a copy of the Safety Data Sheet (SDS), call Elanco Product & Veterinary Support at 888-545-5973.

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 *Advantage Multi for Dogs* has not been established in breeding, pregnant, or lactating dogs. The safe use of *Advantage 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 *Advantage 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 *Advantage Multi for Dogs* has not been evaluated when administered on the same day as an adulticide. *Advantage 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 *Advantage Multi for Dogs*, the microfilaria count in some heartworm-positive dogs may increase or remain unchanged following treatment with *Advantage Multi for Dogs* alone or in a dosing regimen with melarsomine dihydrochloride.

(See ADVERSE REACTIONS and ANIMAL SAFETY – Safety Study in Heartworm-Positive Dogs.)

Advantage 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 *Advantage Multi for Dogs* or an active control, dog owners reported the following post-treatment reactions:

OBSERVATION	Advantage Multi 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, *Advantage Multi for Dogs* 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 *Advantage Multi for Dogs* 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 *Advantage Multi for Dogs*. 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 *Advantage Multi for Dogs*.

The following clinical observations also occurred in laboratory effectiveness studies following application with *Advantage Multi for Dogs* 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 *Advantage Multi for Dogs* 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 *Advantage Multi for Dogs* alone or in a dosing regimen with melarsomine dihydrochloride.

Following treatment with *Advantage Multi for Dogs* alone or in a dosing regimen with melarsomine dihydrochloride, the following adverse reactions were observed:

Adverse Reaction	Dogs Treated with Advantage Multi for Dogs Only n = 106	Dogs Treated with Advantage Multi for Dogs + 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 *Advantage Multi for Dogs* in a dosing regimen with melarsomine dihydrochloride died of pulmonary embolism from dead and dying heartworms. One dog, treated with *Advantage Multi for Dogs* and melarsomine dihydrochloride, experienced pulmonary hemorrhage and responded to supportive medical treatment. Following the first treatment with *Advantage Multi for Dogs* alone, two dogs experienced adverse reactions (coughing, vomiting, and dyspnea) that required hospitalization. In both groups, there were more adverse reactions to *Advantage Multi for Dogs* following the first treatment than the second treatment.

To report a suspected adverse reaction, call 888-545-5973.

Post-Approval Experience (2022)
The following adverse events are based on post-approval adverse drug experience reporting for *Advantage Multi for Dogs*. Not all adverse events 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 reported in dogs are listed in decreasing order of reporting frequency: depression/lethargy, pruritus, vomiting, diarrhea, anorexia, application site reactions (alopecia, pruritus, erythema, and lesions, including blisters), hyperactivity, ataxia, trembling, seizures, panting, hypersalivation, anaphylaxis/anaphylactic reactions (hives, facial swelling, edema of the head), and corneal ulceration.

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.

Contact Information:
For product questions, to report adverse drug experiences, or for a copy of the Safety Data Sheet (SDS), call Elanco Product & Veterinary Support at 888-545-5973.

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

ANIMAL SAFETY:
Heartworm-Negative Dogs
Field Study: In a controlled, double-masked, field safety study, *Advantage Multi for Dogs* was administered to 128 dogs of various breeds, 3 months to 15 years of age, weighing 4 to 157 pounds. *Advantage Multi for Dogs* 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 *Advantage Multi for Dogs*: pruritus, flaky/greasy residue at the treatment site, medicinal odor, lethargy, inappetence, and hyperactivity.

(See ADVERSE REACTIONS.)

Safety Study in Puppies: *Advantage Multi for Dogs* 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: *Advantage Multi for Dogs* 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: *Advantage Multi for Dogs* 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: *Advantage Multi for Dogs* 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: *Advantage Multi for Dogs* 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: *Advantage Multi for Dogs* 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 4 °C (39 °F) and 25 °C (77 °F), avoiding excess heat or cold.

HOW SUPPLIED:

Applications Per Package

6 x 0.4 mL tubes

6 x 1.0 mL tubes

6 x 2.5 mL tubes

6 x 4.0 mL tubes

6 x 5.0 mL tubes

Revised: January 2023

Approved by FDA under NADA # 141-251

Made in Germany

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Manufactured for:

Elanco US Inc

Greenfield, IN 46140 U.S.A.

