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FREEDOM OF INFORMATION SUMMARY

Supplemental NADA 141-189

**ProHeart[®] 6 (moxidectin) Sustained Release
Injectable for Dogs**

**Additional indication for the treatment of existing larval and
adult hookworm (*Uncinaria stenocephala*) infections**

Sponsored by:

Fort Dodge Animal Health

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Freedom of Information Summary
Supplemental NADA 141-189

I. General Information

NADA Number: 141-189

Sponsor: Fort Dodge Animal Health
Division of American Home Products Corporation
800 Fifth Street NW
Fort Dodge, Iowa 50501

Generic Name: Moxidectin

Tradename: ProHeart[®] 6 (moxidectin) Sustained Release Injectable for Dogs

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

Effect of Supplement: New indication for the treatment of existing larval and adult hookworm (*Uncinaria stenocephala*) infections.

II. Indications for Use

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis*.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

III. Dosage Form, Route of Administration and Dosage:

Dosage Form:

ProHeart 6 (moxidectin) is provided in two separate vials that require mixing prior to use. Vial 1 contains 10% moxidectin microspheres and Vial 2 contains a specifically formulated vehicle. Constitution of the moxidectin microspheres in Vial 1 with the vehicle in Vial 2 must be done precisely as directed in the product labeling. No other diluent should be used to constitute Vial 1. The constituted suspension is ready for administration 30 minutes after mixing.

Route of Administration:

The constituted product is intended for subcutaneous administration with an 18G or 20G hypodermic needle in the left or right side of the dorsum of the neck cranial to the scapula. No more than 3.0 mL should be administered in a single site. The location(s) of each injection (left or right side) should be noted so that prior injection sites can be identified and the next injection can be administered on the opposite side.

Dosage:

The constituted product is administered at the dose of 0.05 mL/kg body weight (0.0227 mL/lb) which provides 0.17 mg moxidectin/kg body weight (0.0773 mg/lb). To ensure accurate dosing, calculate each dose based on the dog's weight at the time of treatment. Do not overdose growing puppies in anticipation of their expected adult weight. A dosage chart is included in the labeling to aid in determining the correct dose volume to be administered based on the dog's weight.

IV. Effectiveness

An original new animal drug application for ProHeart 6 (moxidectin) Sustained Release Injectable for Dogs (NADA 141-189) was approved on June 6, 2001 (66 FR 35756, July 9, 2001). All aspects of this NADA 141-189 drug approval are codified in 21 CFR 522.1451. The studies demonstrating the effectiveness of ProHeart 6 against all parasites listed in the originally approved labeling when administered at the recommended 0.17 mg moxidectin/kg body weight dose level are summarized in the original June 6, 2001 NADA 141-189 Freedom of Information Summary. This NADA 141-189 supplement provides additional data confirming the effectiveness of a single administration of ProHeart 6 at the currently approved 0.17 mg/kg body weight dose rate against existing infections of larval and adult *Uncinaria stenocephala*.

Dose Confirmation – Hookworms (*Uncinaria stenocephala*)

The effectiveness of a single subcutaneous injection of ProHeart 6 at the recommended 0.17 mg moxidectin/kg body weight dose rate against larval and adult *Uncinaria stenocephala* infections present at the time of treatment was evaluated in four dose confirmation studies. Three of the four studies evaluated multiple parasites. Results are presented only for *U. stenocephala*.

1. Study Number 0899-C-US-16-99

Title: Efficacy of Moxidectin Canine SR Injectable against Experimental Hookworm Infections in Dogs in Michigan

Type of Study: Laboratory study with induced infections

Purpose: The purpose of this study was to evaluate the effectiveness of the recommended 0.17 mg moxidectin/kg body weight dose rate of ProHeart 6 against experimental infections of the larval and adult stages of two canine hookworm species (*Ancylostoma caninum* and *Uncinaria stenocephala*).

Clinical Investigator: Dwight D. Bowman
Cornell University
Ithaca, NY 14853
(Test facility location: Stanwood, Michigan)

Animals: A total of 30 purpose-bred beagle dogs (15 males and 15 females) weighing between 6.92 to 12.54 kg at the time of treatment were used in this study.

Dosage Groups (10 dogs per group):

Controls treated with saline solution on Day 6 and Day 28 post-infection.

0.17 mg moxidectin/kg body weight on Day 6 post-infection. Second treatment with saline solution on Day 28 post-infection body.

0.17 mg moxidectin/kg body weight on Day 28 post-infection. Initial treatment with saline solution on Day 6 post-infection.

Route of Administration: Subcutaneous injection on the left side of the neck.

Study Duration: 42 days (experimental infection to necropsy).

Study Design: All dogs were determined to be free from hookworm infection by fecal eggs per gram (EPG) prior to initiation of the experiment. Dogs were infected with 200 L₃ *A. caninum* and 400 L₃ *U. stenocephala* on Day 0. Following treatment on Day 6 and Day 28, dogs were observed at approximately 3, 6 and 24 hours post-treatment for any signs of adverse reaction to treatment. Observations for general health were made once daily on all other days. The Day 6 and Day 28 treatments were designed to furnish data pertaining to the effectiveness of the drug against the larval and adult stages (respectively) of these two canine hookworm species. Dogs were sacrificed on Day 42 and their gastrointestinal tracts were processed for nematode recovery and quantification.

Results: Based on the worm counts of control dogs at necropsy, both the *Ancylostoma caninum* and *Uncinaria stenocephala* infections were adequate for evaluation.

Table 1: Effectiveness Against *Uncinaria stenocephala*

Parasite	Treatment	Geometric Mean	% Effectiveness
<i>U. stenocephala</i>	Control	28.5	
	Moxidectin – Day 6	0.0	100.0% (larvae)
	Moxidectin – Day 28	0.0	100.0% (adults)

Conclusion: A single subcutaneous injection of ProHeart 6 given at the recommended dose level of 0.17 mg moxidectin/kg body weight was $\geq 90\%$ effective in the treatment of larval and adult stages of *Uncinaria stenocephala*.

Adverse Reactions: No adverse reactions to treatment were reported. No injection site abnormalities were reported at any observation time.

2. Study Number 0899-C-US-17-99

Title: Efficacy of Moxidectin Canine SR Injectable against Experimental Infections of Hookworms and Whipworms in Dogs in Michigan

Type of Study: Laboratory study with induced infections

Purpose: The purpose of this study was to evaluate the effectiveness of the recommended 0.17 mg moxidectin/kg body weight dose rate of ProHeart 6 against experimental infections of the larval and adult stages of the canine whipworm (*Trichuris vulpis*) and two canine hookworm species (*Ancylostoma caninum* and *Uncinaria stenocephala*).

Clinical Investigator: Dwight D. Bowman
Cornell University
Ithaca, NY 14853
(Test facility location: Stanwood, Michigan)

Animals: A total of 40 purpose-bred beagle dogs (20 males and 20 females) weighing between 8.82 to 16.80 kg at the time of treatment were used in this study.

Dosage Groups (10 dogs per group):

Two controls groups administered saline solution on Days 42 or 91 post-infection.

Two groups given 0.17 mg moxidectin/kg body weight on Days 42 or 91 post-infection with *T. vulpis*.

Route of Administration: Subcutaneous injection on the left side of the neck.

Study Duration: 49 and 105 days (from experimental infection with *T. vulpis* to necropsy).

Study Design: All dogs were determined to be free from hookworm and whipworm infections by fecal EPG prior to initiation of the experiment. All dogs were infected with 500 embryonated *T. vulpis* eggs on Day 0. All dogs were subsequently infected with 200 L₃ *A. caninum* on Day 36 and dogs from only one treated and one control group were infected with 200 L₃ *U. stenocephala* on Days 37. The dogs in the two groups infected with *T. vulpis*, *A. caninum* and *U. stenocephala* were treated approximately a week later on Day 42. These two groups of dogs were sacrificed seven days after treatment on Day 49 and their gastrointestinal tracts were processed for nematode recovery and quantification. The remaining two groups of *A. caninum* and *T. vulpis*-infected dogs were treated on Day 91 and sacrificed 14 days later on Day 105 for nematode recovery and quantification. All dogs were observed at approximately 3, 6 and 24 hours post-treatment for any signs of adverse reaction to treatment. Observations for general health were made once daily on all other days.

Results: Based on the worm counts of control dogs at necropsy, only the *Ancylostoma caninum* and *Uncinaria stenocephala* infections were adequate for evaluation. The effectiveness calculated from the comparison of the group of *Uncinaria stenocephala*-infected dogs treated with ProHeart 6 and the associated control group in this study is shown below.

Table 2: Effectiveness Against *Uncinaria stenocephala* Larvae

Parasite	Treatment	Geometric Mean	% Effectiveness
<i>U. stenocephala</i> larvae	Control	13.64	
	Moxidectin	0.07	99.5%

Conclusion: A single subcutaneous injection of ProHeart 6 given at the recommended dosage of 0.17 mg moxidectin/kg body weight was $\geq 90\%$ effective in the treatment of larval stages of *Uncinaria stenocephala*.

Adverse Reactions: No adverse reactions to treatment were reported. No injection site abnormalities were reported at any observation time.

3. Study Number 0899-C-US-18-99

Title: Efficacy of Moxidectin Canine SR Injectable against Larval/Immature Stages of Experimental *Trichuris vulpis* (Whipworms), *Ancylostoma caninum* and *Uncinaria stenocephala* (Hookworms) Infections in Dogs in New Jersey

Type of Study: Laboratory study with induced infections

Purpose: The purpose of this study was to evaluate the effectiveness of the recommended 0.17 mg moxidectin/kg body weight dose rate of ProHeart 6 against experimental infections of the larval and adult stages of the canine whipworm (*Trichuris vulpis*) and the larval stages of two canine hookworm species (*Ancylostoma caninum* and *Uncinaria stenocephala*).

Clinical Investigator: Sivaja Ranjan
Fort Dodge Animal Health
Princeton, NJ 08543
(Test facility location: Monmouth Junction New Jersey)

Animals: A total of 36 purpose-bred beagle dogs (18 males and 18 females) weighing between 8.20 to 11.85 kg at the time of treatment were used in this study.

Dosage Groups (9 dogs per group):

Two control groups administered saline solution on Day 42 post-infection with *T. vulpis* (five and six days post-infection with *U. stenocephala* and *A. caninum*, respectively).

Two groups treated with 0.17 mg moxidectin/kg body weight on Day 42 post-infection with *T. vulpis* (five and six days post-infection with *U. stenocephala* and *A. caninum*, respectively).

Route of Administration: Subcutaneous injection on the left side of the neck.

Study Duration: 49 and 56 days (from experimental infection with *T. vulpis* to necropsy).

Study Design: All dogs were determined to be free from hookworm and whipworm infections by fecal EPG prior to initiation of the experiment. Dogs were infected with 500 embryonated *T. vulpis* eggs on Day 0. Dogs were subsequently infected with 200 L₃ *A. caninum* on Day 36 and 200 L₃ *U. stenocephala* on Days 37. All groups were treated on Day 42 when all nematodes were in larval or immature stages of development. Following treatment on Day 42, dogs were observed at approximately 3, 6 and 24 hours post-treatment for any signs of adverse reaction to treatment. Observations for general health were made once daily on all other days. One group of treated and one group of control dogs were sacrificed on Day 49 (seven days post-treatment) and their gastrointestinal tracts were processed for nematode recovery and quantification. The remaining groups of treated and control dogs were sacrificed on Day 56 (14 days post-treatment) and identically processed for nematode recovery and quantification.

Results: Based on the worm counts of control dogs at necropsy only the *Ancylostoma caninum* and *Uncinaria stenocephala* infections were adequate for evaluation. The effectiveness calculations for the two *Uncinaria stenocephala* larval infections evaluated in this study are presented below.

Table 3: Effectiveness Against *Uncinaria stenocephala* Larvae

Parasite	Treatment	Geometric Mean	% Effectiveness
<i>U. stenocephala</i> larvae (7 days posttreatment)	Control	21.0	
	Moxidectin	0.2	99.0%
<i>U. stenocephala</i> larvae (14 days posttreatment)	Control	45.4	
	Moxidectin	0.0	100%

Conclusion: A single subcutaneous injection of ProHeart 6 given at the recommended dosage of 0.17 mg moxidectin/kg body weight was $\geq 90\%$ effective in the treatment of the larval stages of *Uncinaria stenocephala*.

Adverse Reactions: No adverse reactions to treatment were reported. No injection site abnormalities were reported at any observation time.

4. Study Number 0899-C-US-19-99

Title: Efficacy of Moxidectin Canine SR Injectable against Experimental Infections of *Uncinaria stenocephala* in Dogs in Georgia

Type of Study: Laboratory study with induced infections

Purpose: The purpose of this study was to evaluate the effectiveness of the recommended 0.17 mg moxidectin/kg body weight dose rate of ProHeart 6 in dogs experimentally infected with *Uncinaria stenocephala*.

Clinical Investigator: John McCall, Ph.D.
TRS Labs, Inc.
Athens, GA 30605
(Test facility location: Athens, Georgia)

Animals: A total of 30 purpose-bred beagle dogs (6 males and 24 females) weighing between 7.15 to 13.30 kg were used in this study.

Dosage Groups (10 dogs per group):

Controls treated with saline solution on Days 6 and 28 post-infection.

0.17 mg moxidectin/kg body weight on Day 6 post-infection and saline solution on Day 28 post-infection.

0.17 mg moxidectin/kg body weight on Day 28 post-infection and saline solution on Day 6 post-infection.

Route of Administration: Subcutaneous injection on the left side of the neck.

Study Duration: 42 days (from experimental infection to necropsy).

Study Design: All dogs were determined to be free from hookworm infection by fecal EPG prior to initiation of the experiment. Dogs were infected with 400 L₃ *U. stenocephala* on Day 0. Following treatment on Day 6 and Day 28, dogs were observed at approximately 3, 6 and 24 hours post-treatment for any signs of adverse reaction to treatment. Observations for general health were made once daily on all other days. Dogs were sacrificed on Day 42 and their gastrointestinal tracts were processed for nematode recovery and quantification.

Results: Based on the worm counts of control dogs at necropsy, *Uncinaria stenocephala* infections were adequate for evaluation. The percent effectiveness reported in the dogs treated on Day 6 post-infection is indicative of effectiveness against larval stages of *U. stenocephala*. The percent effectiveness reported in the dogs treated on Day 28 post-infection is indicative of effectiveness against adult *U. stenocephala*. The effectiveness calculated for both larval and adult stage *U. stenocephala* infections in this study is shown below.

Table 4: Effectiveness Against *Uncinaria stenocephala*

Parasite	Treatment	Geometric Mean	% Effectiveness
<i>U. stenocephala</i>	Control	225.4	
	Moxidectin – Day 6	0.93	99.6% (larvae)
	Moxidectin – Day 28	1.24	99.5% (adults)

Conclusion: A single subcutaneous injection of ProHeart 6 given at the recommended dosage of 0.17 mg moxidectin/kg body weight was $\geq 90\%$ effective in the treatment of larval and adult stages of *Uncinaria stenocephala*.

Adverse Reactions: No adverse reactions to treatment were reported. No injection site abnormalities were reported at any observation time.

V. Animal Safety

The approval of this supplemental NADA 141-189 is for a new indication. It does not change the dose level, frequency or route of administration of ProHeart 6 (moxidectin) Sustained Release Injectable for Dogs or the class or species of treated animals. Consequently, no additional animal safety data were required for approval of this new indication.

VI. Human Safety

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this supplemental NADA. This drug is to be labeled for use in dogs, which are non-food animals.

Human Warnings are provided on the product label as follows:

“Not for human use. Keep this and all drugs out of the reach of children. May be slightly irritating to the eyes. May cause slight irritation to the upper respiratory tract if inhaled. May be harmful if swallowed. If contact with the eyes occurs, rinse thoroughly with water for 15 minutes and seek medical attention immediately. If accidental ingestion occurs, contact a Poison Control Center or a physician immediately. The material safety data sheet (MSDS) contains more detailed occupational safety information.”

VII. Agency Conclusions

The data in support of this NADA comply with the requirements of Section 512 of the Act and Section 514 of the implementing regulations. The data demonstrate that ProHeart 6 (moxidectin) Sustained Release Injectable for Dogs, when used under labeled conditions of use, is safe and effective in the treatment of existing larval and adult infections of *Uncinaria stenocephala*.

The drug is restricted to use by or on the order of a licensed veterinarian because professional expertise is required to determine the existence of heartworm infections, to monitor the safe use of the product and to administer the injectable product.

Under section 512(c)(2)(F)(iii) of the FDCA, this approval for non-food-producing animals qualifies for THREE years of marketing exclusivity beginning on the date of approval because the application contains substantial evidence of the effectiveness of the drug involved or any studies of animal safety required for the approval of the application and conducted or sponsored by the applicant.

Fort Dodge holds Patent No. 4916154 for moxidectin which expires on April 10, 2007.

VIII. Labeling (Attached)

- A. Package Insert
- B. Vials (microspheres and vehicle)
- C. Box



NADA 141-189, Approved by FDA



ProHeart® 6 (moxidectin)

Sustained Release Injectable for Dogs

CAUTION

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

DESCRIPTION

ProHeart 6 (moxidectin) Sustained Release Injectable consists of two separate vials. Vial 1 contains 10% moxidectin sterile microspheres and Vial 2 contains a specifically formulated sterile vehicle for constitution with Vial 1. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains 3.4 mg moxidectin, 3.1% glyceryl tristearate, 2.4% hydroxypropyl methylcellulose, 0.87% sodium chloride, 0.17% methylparaben, 0.02% propylparaben and 0.001% butylated hydroxytoluene. Hydrochloric acid is used to adjust pH.

PHARMACOLOGY

Moxidectin is a semi-synthetic methoxime derivative of nemadectin which is a fermentation product of *Streptomyces cyaneogriseus* subsp. *nancyanogenus*. Moxidectin is a pentacyclic 16-membered lactone macrolide.

Moxidectin has activity resulting in paralysis and death of affected parasites. The stage of the canine heartworm affected at the recommended dose rate of 0.17 mg moxidectin/kg body weight is the tissue larval stage. The larval and adult stages of the canine hookworms, *Ancylostoma caninum* and *Uncinaria stenocephala*, are susceptible.

Following injection with ProHeart 6, peak moxidectin blood levels will be observed approximately 7-14 days after treatment. At the end of the six month dosing interval, residual drug concentrations are negligible. Accordingly, little or no drug accumulation is expected to occur with repeated administrations.

INDICATIONS

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis*.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

DOSAGE AND ADMINISTRATION

Frequency of Treatment: ProHeart 6 prevents infection by *D. immitis* for six months. It should be administered within one month of the dog's first exposure to mosquitoes. Follow-up treatments may be given every six months if the dog has continued exposure to mosquitoes. When replacing another heartworm preventive product, ProHeart 6 should be given within one month of the last dose of the former medication.

ProHeart 6 eliminates the larval and adult stages of *A. caninum* and *U. stenocephala* present at the time of treatment. However, persistent effectiveness has not been established for this indication. Re-infection with *A. caninum* and *U. stenocephala* may occur sooner than 6 months.

Dose: The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb.). This amount of suspension will provide 0.17 mg moxidectin/kg bodyweight (0.0773 mg/lb.). To ensure accurate dosing, calculate each dose based on the dog's weight at the time of treatment. Do not overdose growing puppies in anticipation of their expected adult weight. The following dosage chart may be used as a guide.

DOSAGE CHART

Dog Wt.		Dose Volume	Dog Wt.		Dose Volume
lb	kg	mL/Dog	lb	kg	mL/Dog
11	5	0.25	77	35	1.75
22	10	0.50	88	40	2.00
33	15	0.75	99	45	2.25
44	20	1.00	110	50	2.50
55	25	1.25	121	55	2.75
66	30	1.50	132	60	3.00

Injection Technique: The two-part sustained release product must be mixed at least 30 minutes prior to the intended time of use (See **CONSTITUTION PROCEDURES** for initial mixing instructions). Once constituted, swirl the bottle gently before every use to uniformly re-suspend the microspheres. Withdraw 0.05 mL of suspension/kg body weight into an appropriately sized syringe fitted with an 18G or 20G hypodermic needle. Dose promptly after drawing into dosing syringe. If administration is delayed, gently roll the dosing syringe prior to injection to maintain a uniform suspension and accurate dosing.

Using aseptic technique, inject the product subcutaneously in the left or right side of the dorsum of the neck cranial to the scapula. No more than 3 mL should be administered in a single site. The location(s) of each injection (left or right side) should be noted so that prior injection sites can be identified and the next injection can be administered on the opposite side.

CONTRAINDICATIONS

ProHeart 6 is contraindicated in animals previously found to be hypersensitive to this drug.

HUMAN WARNINGS

Not for human use. Keep this and all drugs out of the reach of children.

May be slightly irritating to the eyes. May cause slight irritation to the upper respiratory tract if inhaled. May be harmful if swallowed. If contact with the eyes occurs, rinse thoroughly with water for 15 minutes and seek medical attention immediately. If accidental ingestion occurs, contact a Poison Control Center or a physician immediately. The material safety data sheet (MSDS) contains more detailed occupational safety information.

PRECAUTIONS

Use with caution in sick, debilitated or underweight animals (see SAFETY).

ProHeart 6 should not be used more frequently than every 6 months.

The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.

Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at three times the labeled dose. Higher doses were not tested.

ADVERSE REACTIONS

In field studies, the following adverse reactions were observed in approximately 1% of 280 dogs treated with ProHeart 6: vomiting, diarrhea, listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature.

Post-Approval Experience: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/toid reactions, depression/lethargy, urticaria, and head/facial edema. As with anaphylaxis/toid reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8536.

ANIMAL SAFETY

General Safety: ProHeart 6 has been safely administered to a wide variety of healthy dogs six months of age and older, including a wide variety of breeds, pregnant and lactating females, breeding males, and ivermectin-sensitive collies. However, in clinical studies, two geriatric dogs with a history of weight loss after the initial ProHeart 6 injection died within a month of the second 6 month injection. A third dog who was underweight for its age and breed and who had a history of congenital problems experienced lethargy following the initial injection of ProHeart 6. The dog never recovered and died 3 months later (see **PRECAUTIONS**).

ProHeart 6 administered at 3 times the recommended dose in dogs with patent heartworm infections and up to 5 times the recommended dose in ivermectin-sensitive collies did not cause any adverse reactions. ProHeart 6 administered at 3 times the recommended dose did not adversely affect the reproductive performance of male or female dogs. ProHeart 6 administered up to 5 times the recommended dose in 7-8 month old puppies did not cause any systemic adverse effects.

In well controlled clinical field studies, ProHeart 6 was safely used in conjunction with a variety of veterinary products including vaccines, anthelmintics, antiparasitics, antibiotics, analgesics, steroids, non-steroidal anti-inflammatory drugs (NSAIDs), anesthetics and flea control products.

Injection Site Reactions: Injection site observations were recorded during effectiveness and safety studies. In clinical studies, ProHeart 6 was administered at six-month intervals to client-owned dogs under field conditions. There were no reports of injection site reactions in these field studies and evaluations of the injection sites revealed no abnormalities.

In a laboratory safety study, ProHeart 6 was administered at 1, 3 and 5 times the recommended dose to 7-8 month old puppies. Injection sites were clipped to facilitate observation. Slight swelling/edema at the injection site was observed in some dogs from all treated groups. These injection site reactions appeared as quickly as 8 hours post injection and lasted up to 3 weeks. A three-year repeated injection study was conducted to evaluate the safety of up to 6 injections of ProHeart 6 administered at the recommended dose (0.17 mg/kg) every 6 months. Mild erythema and localized deep subcuticular thickening were seen in dogs that received four injections in the same area on the neck and in one dog that received two injections in the same area on the neck. Microscopic evaluation on the injection sites from all dogs 6 months after the last injection consistently showed mild granulomatous panniculitis with microvacuolation. The only adverse reaction seen that was not related to the injection site was weight loss in one dog.

Some dogs treated with ProHeart 6 in laboratory effectiveness studies developed transient, localized inflammatory injection site reactions. These injection site reactions were visible grossly for up to 3 weeks after injection. Histologically, well-defined granulomas were observed in some dogs at approximately 5 months after injection.

CONSTITUTION PROCEDURES

The two-part ProHeart 6 product must be mixed at least 30 minutes prior to the intended time of use.

Items needed to constitute ProHeart 6:

- Microspheres (vial 1)
- Enclosed vent needle (25G)
- Vehicle (vial 2)
- Sterile 20 mL syringe for transfer
- Transfer needle (18G or 20G)



Constitution of the 20 mL vial product.

1. Shake the microsphere vial to break up any aggregates prior to constitution.
2. Using an 18G or 20G needle and sterile syringe withdraw 17.0 mL of the unique vehicle from the vial. **There is more vehicle supplied than the 17.0 mL required.**
3. Insert the enclosed 25G vent needle into the microsphere vial.
4. Slowly transfer the vehicle into the microsphere vial through the stopper using the transfer needle and syringe.
5. Once the vehicle has been added, remove the vent and transfer needles from the microsphere vial. Discard unused vehicle and needles.
6. Shake the microsphere vial vigorously until a thoroughly mixed suspension is produced.
7. Record the time and date of mixing on the microsphere vial.
8. Allow suspension to stand for at least 30 minutes to allow large air bubbles to dissipate.
9. Before every use, gently swirl the mixture to achieve uniform suspension. The microspheres and vehicle will gradually separate on standing.
10. Use a 1 mL or 3 mL syringe and an 18G or 20G needle for dosing. Dose promptly after drawing into dosing syringe. If administration is delayed, gently roll the dosing syringe prior to injection to maintain a uniform suspension and accurate dosing.
11. Refrigerate the unused product. The constituted product remains stable for 4 weeks in a refrigerator. Avoid direct sunlight.



STORAGE INFORMATION

Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

HOW SUPPLIED

ProHeart 6 is available in the following two package sizes.

1. 5-Pack

NDC 0856-3670-25 - 20 mL vial product:
5 - 10% moxidectin sterile microspheres - 598 mg/vial
5 - Sterile vehicle - 17 mL/vial

2. 10-Pack

NDC 0856-3670-29 - 20 mL vial product:
10 - 10% moxidectin sterile microspheres - 598 mg/vial
10 - Sterile vehicle - 17 mL/vial

For customer service, product information or to obtain a copy of the MSDS, call (800) 685-5656.

U.S. Patent No. 4,916,154 and 6,340,671

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

598 mg MICROSPHERE VIAI
ACTUAL SIZE

NDC 0856-3670-20
PROHEART
ProHeart*6
(moxidectin)
Sustained Release Injectable for Dogs
18% moxidectin sterile microspheres
598 mg
To be constituted with 17 mL ProHeart 6 vehicle.
CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.
ADA 141-103. Approved by FDA.

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.
The product must be mixed at least 30 minutes prior to the planned time of use.
The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb).
Read accompanying package insert carefully before use.
Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).
U.S. Patent Nos. 4,916,154 and 6,340,871
Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

Date/Time of constitution:
Lot:
Exp. 3673C

17 mL VEHICLE VIAL
ACTUAL SIZE

NDC 0856-2670-20
PROHEART 6
(moxidectin)
Sustained Release Injectable for Dogs
Sterile Vehicle
17 mL

To be used to constitute moxidectin microspheres.
CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.
NADA 141-189. Approved by FDA

PROHEART 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.
There is more vehicle supplied than required for constitution. Read accompanying package insert carefully before use.
Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).
U.S. Patent No. 4,916,154 and 6,340,671

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

Lot
Exp.

CEPHE

1549 mg MICROSPHERE VIAL
ACTUAL SIZE

NDC 0866-3670-50

FORT DODGE

ProHeart⁶

(moxidectin)

Sustained Release Injectable for Dogs
10% moxidectin sterile microspheres

1549 mg

To be constituted with 44 mL ProHeart 6 vehicle.

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

NADA 141-189, Approved by FDA.

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

The product must be mixed at least 30 minutes prior to the intended time of use.

The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb).

Read accompanying package insert carefully before use.

Store unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

U.S. Patent No. 4,916,164 and 6,340,671

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

08663670
9529E

Date here of constitution:
Lot
Exp.

30367510

44 mL VEHICLE VIAL
ACTUAL SIZE

NDC 0856-3670-50

ProHeart⁶
(moxidectin)

Sustained Release Injectable for Dogs
Sterile Vehicle

44 mL

To be used to constitute moxidectin microspheres.

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

NADA 141-189, Approved by FDA

ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

There is more vehicle supplied than required for constitution. Read accompanying package insert carefully before use.

Store unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2 to 8°C (36° to 46°F).

U.S. Patent Nos. 4,916,154 and 6,340,671

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

Lot
Exp

00985
8591E



30368510

INDICATIONS: ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis*.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

STORAGE: Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

U.S. Patent No. 4,916,154 and
6,340,671

Lot

Exp.

NDC 0856-3670-20



ProHeart® 6 (moxidectin)

Sustained Release Injectable for Dogs

1 Vial of Moxidectin Sterile Microspheres 598 mg
1 Vial of Sterile Vehicle 17 mL
1 Vent Needle

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

Read accompanying package insert carefully before use.

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA
NADA 141-189, Approved by FDA

CONTRAINDICATIONS: ProHeart 6 is contraindicated in animals previously found to be hypersensitive to this drug.

DESCRIPTION: ProHeart 6 consists of two separate vials. Vial 1 contains 10% moxidectin sterile microspheres and Vial 2 contains a specifically formulated sterile vehicle for constitution with Vial 1. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains 3.4 mg moxidectin, 3.1% glyceryl tristearate, 2.4% hydroxypropyl methylcellulose, 0.87% sodium chloride, 0.17% methylparaben, 0.02% propylparaben and 0.001% butylated hydroxytoluene. Hydrochloric acid is used to adjust pH.

DOSE: The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb.). This amount of suspension will provide 0.17 mg moxidectin/kg body weight (0.0773 mg/lb.).

PRECAUTIONS: Use with caution in sick, debilitated or underweight animals.

ProHeart 6 should not be used more frequently than every 6 months. The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.

Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at three times the labeled dose. Higher doses were not tested.

ADVERSE REACTIONS: In field studies, the following adverse reactions were observed in approximately 1% of 280 dogs treated with ProHeart 6: vomiting, diarrhea, listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature.

Post-Approval Experience: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/toxic reactions, depression/lethargy, urticaria, and head/face edema. As with anaphylaxis/toxic reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8536.

ProHeart® 6
(moxidectin)
Sustained Release Injectable for Dogs
USE VENT NEEDLE TO CONSTITUTE

9734
00852
3674B

9734
3674B

SMALL VIAL-SIZE
TWIN PACK
ACTUAL SIZE

LARGE VIAL-SIZE
TWIN PACK
ACTUAL SIZE

USE VENT NEEDLE TO CONSTITUTE
Sustained Release Injectable for Dogs
ProHeart® 6
(moxidectin)

PRECAUTIONS: Use with caution in sick, debilitated or underweight animals. ProHeart 6 should not be used more frequently than every 6 months. The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.

Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at three times the labeled dose. Higher doses were not tested.

ADVERSE REACTIONS: In field studies, the following adverse reactions were observed in approximately 1% of 280 dogs treated with ProHeart 6: vomiting, diarrhea, listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature.

Post-Approval Experience: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/toid reactions, depression/lethargy, urticaria, and head/ facial edema. As with anaphylaxis/toid reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8536.

INDICATIONS: ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilaria immitis*.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

STORAGE: Store unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

U.S. Patent No. 4,916,154 and 6,340,671

Lot

Exp.

NDC 0856-3670-50



ProHeart® 6
(moxidectin)

1 Vial of Moxidectin Sterile Microspheres 1549 mg
1 Vial of Sterile Vehicle 44 mL
1 Vent Needle

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

Read accompanying package insert carefully before use.

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA
NADA 141-189; Approved by FDA

CONTRAINDICATIONS: ProHeart 6 is contraindicated in animals previously found to be hypersensitive to this drug.

DESCRIPTION: ProHeart 6 consists of two separate vials. Vial 1 contains 10% moxidectin sterile microspheres and Vial 2 contains a specifically formulated sterile vehicle for constitution with Vial 1. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains 3.4 mg moxidectin, 3.1% glyceryl tristearate, 2.4% hydroxypropyl methylcellulose, 0.87% sodium chloride, 0.17% methylparaben, 0.02% propylparaben and 0.001% butylated hydroxytoluene. Hydrochloric acid is used to adjust pH.

DOSE: The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb.). This amount of suspension will provide 0.17 mg moxidectin/kg body weight (0.0773 mg/lb.).

9735
00852
3676P

9735
3676B

Sustained Release Injectable for Dogs
USE VENT NEEDLE TO CONSTITUTE

ProHeart⁶
(moxidectin)

Fort Dodge Animal Health

List

Exp. Date



FORT DODGE ANIMAL HEALTH



Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

INDICATIONS: ProHeart 6 is indicated for use in dogs 6 months of age and older for the prevention of heartworm disease caused by *Dirofilara immitis*.
ProHeart 6 is indicated for the treatment of existing larval and adult heartworm (Ankylostoma caninum and Uncinaria stenocephala) infections.

STORAGE: Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

CONTRAINDICATIONS: ProHeart 6 is contraindicated in animals previously known to be hypersensitive to this drug.

Read accompanying package insert carefully before use.

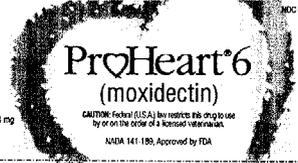
DESCRIPTION: ProHeart 6 consists of two separate vials. Vial 1 contains 10% moxidectin sterile microspheres, and Vial 2 contains a specially formulated sterile vehicle for constitution with Vial 1. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains: 2.4 mg moxidectin, 1.0% phenyl ethanol, 2.4% benzoylarginyl methylamide, 0.3% sodium chloride, 0.17% methylparaben, 0.10% propylene glycol, and 0.01% indelible hydroxybenzoic hydrochloric acid to adjust pH.

DOSE: The recommended subcutaneous dose is 0.05 mL of the constituted suspension per body weight (0.0227 mL/lb). The amount of suspension will provide 0.17 mg moxidectin per body weight (0.0773 mg/lb).



FORT DODGE ANIMAL HEALTH

Sustained Release Injectable for Dogs
5 Vials of Moxidectin Sterile Microspheres 500 mg
5 Vials of Sterile Vehicle 17 mL
5 Vial Needles



CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.
NADA 141-189, Approved by FDA

MOX 0556-3670-25

PRECAUTIONS: Use with caution in sick, debilitated or underweight animals.
ProHeart cannot be used more frequently than every 6 months. The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.
Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.
No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at lower than the labeled dose. Higher doses were not tested.

ADVERSE REACTIONS: In field studies, the following adverse reactions were observed in approximately 1% of 200 dogs treated with ProHeart 6: vomiting, diarrhea, inappetence, weight loss, lethargy, injection site pruritus, and elevated body temperature.
Post-Approval Surveillance: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience monitoring: anaphylactoid reactions, depression, lethargy, anorexia, and focal facial edema. As with any drug, local reactions resulting from the use of viral diagnostic products, standard therapeutic interventions should be initiated immediately.
To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8030.

U.S. Patent Nos. 4,816,154 and 6,340,677

0880
06852
30788
0609
30788



5-PACK CARTON
32% ACTUAL SIZE

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA



S-PACK CARTON
TOP PANEL
ACTUAL SIZE

FORT DODGE ANIMAL HEALTH



Exp. Date

Lot



FORT DODGE ANIMAL HEALTH

ProHeart[®] 6

(moxidectin)

Sustained Release Injectable for Dogs
USE VENT NEEDLE TO CONSTITUTE

5-PACK CARTON
SIDE PANEL
ACTUAL SIZE

INDICATIONS: ProHeart 6 is indicated for use in dogs six months of age and older for the prevention of heartworm disease caused by *Dirofilana immitis*.

ProHeart 6 is indicated for the treatment of existing larval and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections.

STORAGE: Store the unconstituted product at or below 25°C (77°F). Do not expose to light for extended periods of time. After constitution, the product is stable for 4 weeks stored under refrigeration at 2° to 8°C (36° to 46°F).

CONTRAINDICATIONS: ProHeart 6 is contraindicated in animals previously found to be hypersensitive to this drug.

DESCRIPTION: ProHeart 6 consists of two separate vials. Vial 1 contains 10% moxidectin sterile microspheres and Vial 2 contains a specifically formulated sterile vehicle for constitution with Vial 1. No other diluent should be used. A clear or translucent appearance of the vehicle is normal. Each mL of constituted drug product contains 3.4 mg moxidectin, 3.1% glyceryl tristearate, 2.4% hydroxypropyl methylcellulose, 0.37% sodium chloride, 0.17% methylparaben, 0.02% propylparaben and 0.001% butylated hydroxytoluene. Hydrochloric acid is used to adjust pH.

DOSE: The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight (0.0227 mL/lb). This amount of suspension will provide 0.17 mg moxidectin/kg body weight (0.0773 mg/lb).

Read accompanying package insert carefully before use.

FOF

Su:
5 Vi
5 Vi
5 Ve

5-PACK CARTON
FRONT PANEL
ACTUAL SIZE

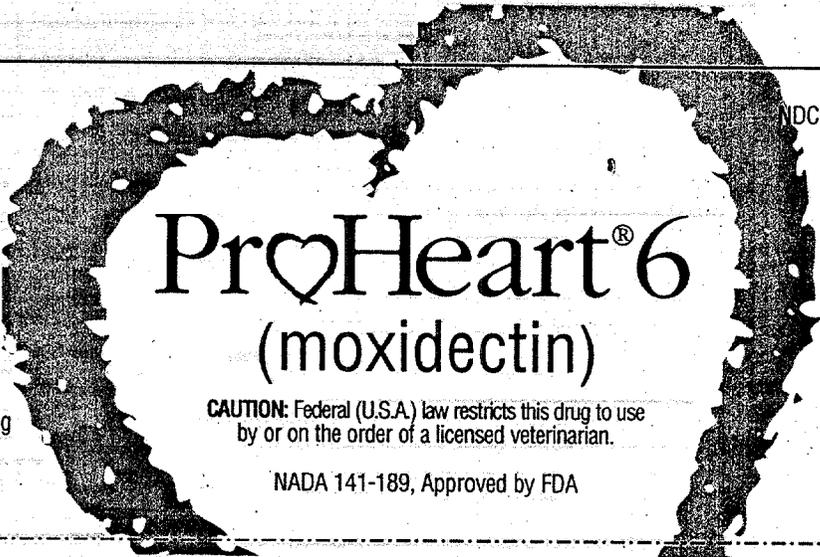


FORT DODGE ANIMAL HEALTH

Sustained Release Injectable for Dogs

5 Vials of Moxidectin Sterile Microspheres 598 mg
5 Vials of Sterile Vehicle 17 mL
5 Vent Needles

NDC 0856-3670-25



ProHeart[®] 6
(moxidectin)

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

NADA 141-189, Approved by FDA



9889
00852
3678B

9889
3678B

9889
3678B

PRECAUTIONS: Use with caution in sick, debilitated or underweight animals.

ProHeart 6 should not be used more frequently than every 6 months. The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.

Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

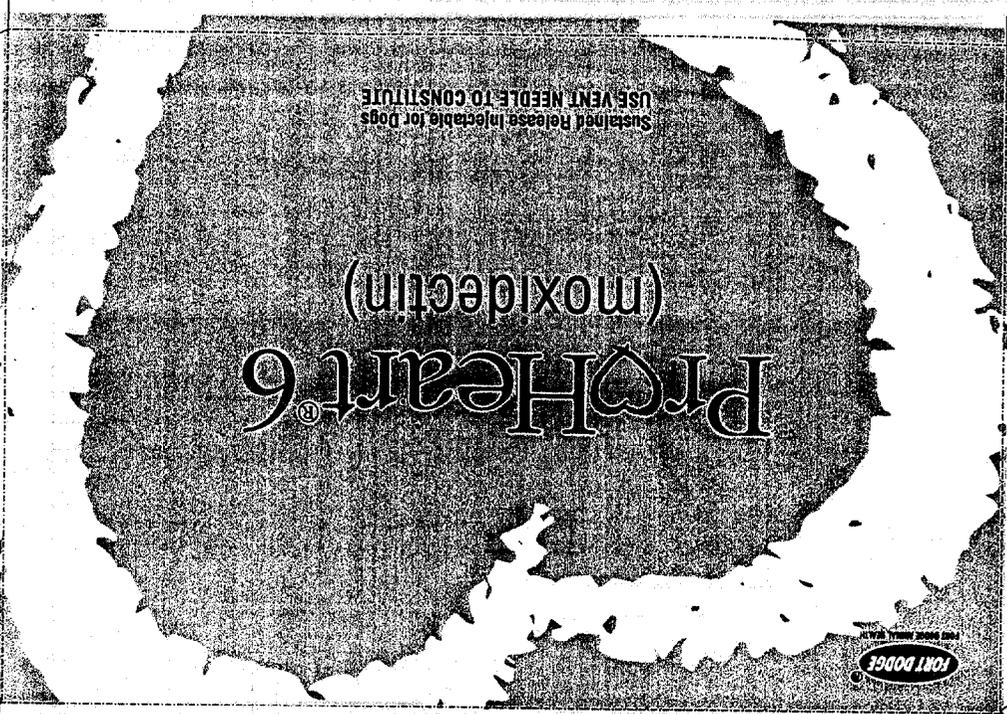
No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at three times the labeled dose. Higher doses were not tested.

ADVERSE REACTIONS: In field studies, the following adverse reactions were observed in approximately 1% of 280 dogs treated with ProHeart 6: vomiting, diarrhea, listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature.

Post-Approval Experience: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/toid reactions, depression/lethargy, urticaria, and head/face edema. As with anaphylaxis/toid reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8536.

U.S. Patent No. 4,916,154 and 6,340,673



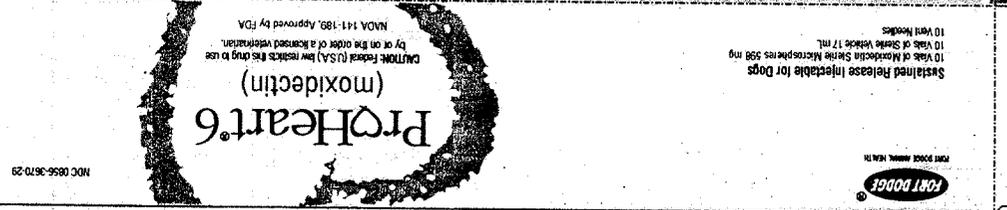
Lot
Exp. Date



Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

ProHeart 6 (moxidectin) is a prescription drug. It is used to prevent heartworm disease, lungworm disease, and intestinal parasites in dogs. It is also used to treat existing infections. ProHeart 6 is a long-acting, sustained-release formulation of moxidectin. It is administered by subcutaneous injection. The active ingredient, moxidectin, is a macrocyclic lactone. It is effective against heartworm disease, lungworm disease, and intestinal parasites. ProHeart 6 is approved for use in dogs 6 weeks of age and older. It is contraindicated in dogs with known hypersensitivity to moxidectin or any of the other ingredients. ProHeart 6 is a prescription drug and should be used only as directed. For more information, please contact your veterinarian.

ProHeart 6 (moxidectin) is a prescription drug. It is used to prevent heartworm disease, lungworm disease, and intestinal parasites in dogs. It is also used to treat existing infections. ProHeart 6 is a long-acting, sustained-release formulation of moxidectin. It is administered by subcutaneous injection. The active ingredient, moxidectin, is a macrocyclic lactone. It is effective against heartworm disease, lungworm disease, and intestinal parasites. ProHeart 6 is approved for use in dogs 6 weeks of age and older. It is contraindicated in dogs with known hypersensitivity to moxidectin or any of the other ingredients. ProHeart 6 is a prescription drug and should be used only as directed. For more information, please contact your veterinarian.





FORT DODGE ANIMAL HEALTH

PROHeart[®] 6 (moxidectin)

10-PACK CARTON
TOP PANEL
90% ACTUAL SIZE

Sustained Release Injectable for Dogs
USE VENT NEEDLE TO CONSTITUTE



FORT DODGE ANIMAL HEALTH

Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

Lot

Exp. Date



10-PACK CARTON
BACK PANEL
90% ACTUAL SIZE

10-PACK CARTON
FRONT PANEL
90% ACTUAL SIZE



FORT DODGE ANIMAL HEALTH

Sustained Release Injectable for Dogs

10 Vials of Moxidectin Sterile Microspheres 598 mg

10 Vials of Sterile Vehicle 17 mL

10 Vent Needles

ProHeart[®] 6
(moxidectin)

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

NADA 141-189, Approved by FDA

NDC 0856-3670-29

10-PACK CARTON
SIDE PANEL
90% ACTUAL SIZE

PRECAUTIONS: Use with caution in sick, debilitated or underweight animals.

ProHeart 6 should not be used more frequently than every 6 months. The safety and effectiveness of ProHeart 6 has not been evaluated in dogs less than 6 months of age.

Prior to administration of ProHeart 6, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. ProHeart 6 is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, ProHeart 6 is not effective for microfilariae clearance.

No adverse reactions were observed in dogs with patent heartworm infections when ProHeart 6 was administered at three times the labeled doses. Higher doses were not tested.

ADVERSE REACTIONS: In field studies, the following adverse reactions were observed in approximately 1% of 280 dogs treated with ProHeart 6: Vomiting, diarrhea, listlessness, weight loss, seizures, injection site pruritus, and elevated body temperature.

Post-Approval Experience: Although not all adverse reactions are reported, the following reactions are based on voluntary post-approval drug experience reporting: anaphylaxis/shock reactions, depression/lethargy, urticaria, and head/face edema. As with anaphylaxis/shock reactions resulting from the use of other injectable products, standard therapeutic intervention should be initiated immediately.

To report suspected adverse reactions or to obtain technical assistance, call (800) 533-8536.

U.S. Patent No. 4,916,164 and 6,340,671

**Freedom of Information Summary
Supplemental NADA 141-189**

cc: ✓ HFV-199, NADA Original
HFV-2 Special Mailing List
HFV-12 FOI Staff
HFV-102 QAT Reserve
HFV-102 Green Book (NTurner)
HFA-305 Dockets Management
KAN-DO, HFR-SW350
Sponsor Copy

ec: CVM Records\ONADE\N141189\C0009foi.sum