HEARTGARD PLUS- ivermectin and pyrantel pamoate tablet, chewable
Boehringer Ingelheim Animal Health USA Inc.

HEARTGARD® PLUS
(ivermectin/pyrantel)

Approved by FDA under NADA # 140-971

Chewables

Caution:

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Indications:

For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of roundworms (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

Dosage:

HEARTGARD® PLUS should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of roundworms and hookworms is as follows:

Dog Weight	Chewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding on Foil Backing and Carton
0 - 25 lbs	1	68 mcg	57 mg	Blue
26 - 50 lbs	1	136 mcg	114 mg	Green
51 - 100 lbs	1	272 mcg	227 mg	Brown

HEARTGARD® PLUS is recommended for dogs 6 weeks of age and older.
For dogs over 100 lbs use the appropriate combination of these chewables.

Administration:

Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light.

Because most dogs find HEARTGARD® PLUS palatable, the product can be offered to the dog by hand. To avoid the risk of choking or intestinal obstruction, the chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing (see *Precautions* and *Post-Approval Experience)*. Alternatively,

it may be added intact to a small amount of dog food to encourage chewing, but care should be taken to ensure that the dog consumes the complete dose at one time.

Treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD® PLUS should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD® PLUS must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD® PLUS and resumption of the recommended dosing regimen minimizes the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD® PLUS also provides effective treatment and control of roundworms (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

Efficacy:

HEARTGARD® PLUS (ivermectin/pyrantel) Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D. immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD® PLUS Chewables are also effective against canine roundworms (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*).

Acceptability:

In acceptability and field trials, HEARTGARD® PLUS was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

Precautions:

All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD® PLUS which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD® PLUS.

While some microfilariae may be killed by the ivermectin in HEARTGARD® PLUS at the recommended dose level, HEARTGARD® PLUS is not effective for microfilariae

clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

Choking or intestinal obstruction has been reported after dosing with HEARTGARD® PLUS. For dogs that normally swallow treats whole, chewables may be broken into pieces (see *Post-Approval Experience*).

Keep this and all drugs out of the reach of children. In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans.

Keep HEARTGARD® PLUS in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Adverse Reactions:

In clinical field trials with HEARTGARD® PLUS, vomiting or diarrhea within 24 hours of dosing was observed (1.1% of administered doses).

Post-Approval Experience (2022): The following adverse events are based on post-approval adverse drug experience reporting for HEARTGARD® PLUS. 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 these data.

The following adverse events reported in dogs are listed in decreasing order of reporting frequency:

Vomiting, diarrhea, lethargy, anorexia, seizures, ataxia, muscle tremors, hypersalivation, pruritus.

In some cases, choking or intestinal obstruction has been reported after administration of HEARTGARD® PLUS.

Contact Information: To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or www.fda.gov/reportanimalae.

Safety:

HEARTGARD® PLUS has been shown to be bioequivalent to HEARTGARD®, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD® PLUS and HEARTGARD® are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD® demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies.

Results of these trials and bioequivalency studies, support the safety of HEARTGARD® products in dogs, including Collies, when used as recommended.

HEARTGARD® PLUS has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD® PLUS in a heartworm disease preventive program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

How Supplied:

HEARTGARD® PLUS is available in three dosage strengths (see *Dosage*) for dogs of different weights. Each strength comes in convenient cartons of 1, 6 and 12 chewables.

Storage Information:

Store between 68° F - 77° F (20° - 25° C). Excursions between 59° F - 86° F (15° - 30° C) are permitted. Protect product from light.

Marketed by:

Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

Rev. 03-2023
151749-005; 162813-003; (1050-1999-07)

PRINCIPAL DISPLAY PANEL – Carton 6 Chewables (For dogs and puppies 0 - 25 LBS)

PRINCIPAL DISPLAY PANEL – Carton 6 Chewables (For dogs and puppies 26 - 50 LBS)

PRINCIPAL DISPLAY PANEL – Carton 6 Chewables (For dogs 51-100 LBS)

HEARTGARD PLUS

ivermectin and pyrantel pamoate tablet, chewable

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0010-4012
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ivermectin (UNII: 8883YP2R6D) (ivermectin - UNII:8883YP2R6D)	ivermectin	68 ug
pyrantel pamoate (UNII: 81BK194Z5M) (pyrantel - UNII:4QIH0N49E7)	pyrantel	57 mg

Product Characteristics

Color	RED (red to red-brown)	**Score**	no score
Shape	RECTANGLE	**Size**	25mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0010-4012-01	1 in 1 CARTON		
1		6 in 1 BLISTER PACK		
2	NDC:0010-4012-02	2 in 1 CARTON		
2		6 in 1 BLISTER PACK		
3	NDC:0010-4012-03	1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:0010-4012-04	1 in 1 CARTON		
4		1 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA140971	04/10/2020	

HEARTGARD PLUS

ivermectin and pyrantel pamoate tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0010-4013
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ivermectin (UNII: 8883YP2R6D) (ivermectin - UNII:8883YP2R6D)	ivermectin	136 ug
pyrantel pamoate (UNII: 81BK194Z5M) (pyrantel - UNII:4QIH0N49E7)	pyrantel	114 mg

Product Characteristics

Color	RED (red to red-brown)	**Score**	no score
Shape	RECTANGLE	**Size**	32mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0010-4013-01	1 in 1 CARTON		
1		6 in 1 BLISTER PACK		
2	NDC:0010-4013-02	2 in 1 CARTON		
2		6 in 1 BLISTER PACK		
3	NDC:0010-4013-03	1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:0010-4013-04	1 in 1 CARTON		
4		1 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA140971	04/10/2020	

HEARTGARD PLUS

ivermectin and pyrantel pamoate tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0010-4014
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ivermectin (UNII: 8883YP2R6D) (ivermectin - UNII:8883YP2R6D)	ivermectin	272 ug
pyrantel pamoate (UNII: 81BK194Z5M) (pyrantel - UNII:4QIH0N49E7)	pyrantel	228 mg

Product Characteristics

Color	RED (red to red-brown)	**Score**	no score
Shape	RECTANGLE	**Size**	38mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0010-4014-01	1 in 1 CARTON		
1		6 in 1 BLISTER PACK		
2	NDC:0010-4014-02	2 in 1 CARTON		
2		6 in 1 BLISTER PACK		
3	NDC:0010-4014-03	1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:0010-4014-04	1 in 1 CARTON		

4		1 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA140971	04/10/2020	

Labeler - Boehringer Ingelheim Animal Health USA Inc. (007134091)

Revised: 10/2023 Boehringer Ingelheim Animal Health USA Inc.