

FRONT

BACK

100 mm



607998001

# Heartgard<sup>®</sup> PLUS

(ivermectin/pyrantel)

## Chewable Tablets

**Description:** Red to red-brown with yellow tinge, characteristic of fresh beef, no rancid, sour, putrid or other abnormal odors but rather a wholesome meaty odor.

**Pharmacology:** The tissue larval stage of *Dirofilaria immitis* is exquisitely sensitive to ivermectin. Since only a small amount of ivermectin is required to eliminate these larvae, the spectrum of activity of Heartgard Plus against other parasites is limited as compared to the ivermectin formulations and doses used in other species.

The action of the avermectins is unique and is not shared by other classes of antiparasitic agents. It involves the neurotransmitter gamma-aminobutyric acid, or GABA. Ivermectin stimulates the release of GABA from nerve endings and enhances binding of GABA to receptors at nerve junctions, thus interrupting nerve impulses and thereby paralyzing and killing the sensitive heartworm larvae.

The recommended heartworm preventive dose of ivermectin has a wide safety margin in dogs. The action of the principal peripheral neurotransmitter in mammals, acetylcholine, is unaffected by ivermectin. In mammals, ivermectin does not readily penetrate the central nervous system where GABA functions as a neurotransmitter.

Pyrantel depolarizes the muscle membrane and increases spike-discharge frequency. Paralyzed worms are expelled from the gastro-intestinal tract by normal peristalsis.

Two pharmacokinetics trials demonstrated the relative bioequivalence of ivermectin in Heartgard tablets and ivermectin in chewable formulation containing both ivermectin and pyrantel pamoate. The first trial demonstrated adequate absorption of ivermectin from a beef-based chewable formulation when compared to Heartgard tablets. The chewable formulation of ivermectin was similar to the tablet formulation with respect to the bioavailability of ivermectin. The second trial demonstrated that pyrantel did not interfere with the absorption of ivermectin when combined in a beef-based chewable vehicle. The presence of pyrantel pamoate in the chewable formulation did not interfere with the absorption of ivermectin.

The pamoate salt of pyrantel is poorly soluble in water, which offers the advantage of reduced absorption from the gut, allowing the drug to reach lower end of the large intestine in dogs, cats and equines.

**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 ascarides (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

**Dosage:** HEARTGARD<sup>®</sup> 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 ascarides and hookworms is as follows:

Dog Weight	Chewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding on Foil Backing and Carton
Up to 11kg	1	68 mcg	57 mg	Blue
12 - 22kg	1	136 mcg	114 mg	Green
23 - 45kg	1	272 mcg	227 mg	Brown

HEARTGARD<sup>®</sup> PLUS is recommended for dogs 6 weeks of age and older. For dogs over 45kg 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<sup>®</sup> PLUS palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and 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 dose has been lost, redosing is recommended.

HEARTGARD<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> PLUS and resumption of the recommended dosing regimen minimizes the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD<sup>®</sup> PLUS also provides effective treatment and control of ascarides (*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.

**Acceptability:** In acceptability and field trials, HEARTGARD<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> PLUS.

While some microfilariae may be killed by the ivermectin in HEARTGARD<sup>®</sup> PLUS at the recommended dose level, HEARTGARD<sup>®</sup> 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.

**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.

Drug containers and any residual contents should be disposed of safely so as to respect the environment and according to the legislation of the country.

Do not store above 25°C. Protected from light.

**Adverse Reactions:** In clinical field trials with HEARTGARD<sup>®</sup> PLUS, vomiting or diarrhea within 24 hours of dosing was observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD<sup>®</sup>: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

**Safety:** HEARTGARD<sup>®</sup> PLUS has been shown to be bioequivalent to HEARTGARD<sup>®</sup>, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD<sup>®</sup> PLUS and HEARTGARD<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> products in dogs, including Collies, when used as recommended.

HEARTGARD<sup>®</sup> 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 vaccines, antibiotics, flea control preparations (dips, collars, mists, shampoos, etc), steroids, vitamins, cestocides, anti-inflammatories, anesthetics, tranquilizers, ophthalmic medications and hormone preparations have been administered with HEARTGARD<sup>®</sup> 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.

Clinical studies have shown a wide margin of safety at the recommended dose level. In case of toxicity, symptomatic and supportive treatment is recommended.

**How Supplied:** HEARTGARD<sup>®</sup> PLUS is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 chewables.

**Manufactured by:** Boehringer Ingelheim Animal Health Puerto Rico LLC, Rd #2 KM 56.7, Barceloneta, Puerto Rico 00617 USA

**Product Owner:** Boehringer Ingelheim Vetmedica GmbH, Binger Straße 173, 55216 Ingelheim am Rhein, Germany

**Registration holder:** Rhone Ma Malaysia Sdn Bhd (200001023275), Lot 18A & 18B, Jalan 241, Seksyen 51A, 46100 Petaling Jaya, Selangor, Malaysia

©2023 Boehringer Ingelheim Animal Health USA Inc.

All rights reserved.

5LHEAPS3-006 06/XXX

Date of revision: 15/08/23  
607998-001



	<b>Code: 607998-001</b>
GO DUL	SAP #: 184060, 184061, 184062
INITIALS: RP	Version: 3 <b>15AUG23</b>

<b>Product Component Type Size:</b>	<b>Heartgard PLUS Insert</b>
<b>Country(s):</b>	Malaysia (MA)
<b>Dimensions Flat:</b>	100 x 200 mm
<b>Dimensions Folded:</b>	N/A
<b>Template #:</b>	N/A
<b>Corner Radius:</b>	N/A

<b>DIELINE:</b>	N/A
-----------------	-----

<b>CANCEL &amp; REPLACE:</b>	NA
------------------------------	----

<b>Notes for BAR site:</b>	NA
----------------------------	----

## COLORS

BLACK