

HEARTGARD® Plus (ivermectin/pyrantel):

The #1 veterinarian-recommended heartworm preventive.¹

HEARTGARD Plus gives dog owners peace of mind because it has nearly a 20-year history² of safety and efficacy and over 2.1 billion doses have been sold, worldwide.³

How does HEARTGARD Plus work?

HEARTGARD Plus not only prevents heartworm disease but also treats and controls the most common intestinal parasites, hookworms and roundworms. It contains 2 medications: ivermectin and pyrantel pamoate.

Ivermectin prevents heartworm disease by killing heartworm larvae that have infected your dog during the previous 30 days. By killing the larvae, HEARTGARD Plus stops larvae from developing into juvenile and adult heartworms, thereby preventing the disease.

The low dose of ivermectin is metabolized and excreted rapidly, so it kills heartworm larvae present today but does not have an effect on larvae introduced tomorrow.⁴ That is why it is recommended to administer HEARTGARD Plus every 30 days.

Pyrantel pamoate kills roundworms and hookworms living in your dog's intestines. The use of HEARTGARD Plus every month may help to reduce the burden of roundworm eggs and hookworm larvae in the environment, and thereby reduce the risk of reinfection.



Why do dog owners prefer the Real-Beef Chewable vs. a pill?

HEARTGARD Plus is the only FDA-approved heartworm preventive offering a unique combination of real beef and a soft chew dogs love to take. In preference tests, dogs preferred HEARTGARD Plus chewables by a margin of 37 to 1 over the next leading brand.⁵ In a survey, 1 out of 5 pet owners reported later finding the heartworm pill they thought their dog had swallowed.⁶ HEARTGARD Plus gives owners confidence the dog will accept the product.



To protect your dog against heartworm disease as well as treat and control hookworms and roundworms, choose the #1 vet-recommended brand,¹ HEARTGARD Plus. Make sure you give it to your dog every 30 days, all year long, as recommended by the American Heartworm Society.⁷

Important Safety Information:

HEARTGARD (ivermectin) is well tolerated. All dogs should be tested for heartworm infection before starting a preventive program. Following the use of HEARTGARD, digestive and neurological side effects have rarely been reported. For more information, please visit www.HEARTGARD.com.

¹ Market Dynamics: Share report monthly canine heartworm preventives, vet-dispensed treatment; Data on file at Merial

² HEARTGARD tablet was launched in 1987 and HEARTGARD Plus was launched in 1993.

³ Data on file at Merial

⁴ Campbell WC. Use of ivermectin in dogs and cats. In: Campbell WC, ed. *Ivermectin and Abamectin*. New York: Springer-Verlag, 1989:246-248.

⁵ Of dogs showing a preference in three studies conducted by independent investigators, dogs preferred HEARTGARD (ivermectin) Chewables over INTERCEPTOR® (milbemycin oxime) Flavourtabs® by a margin of 37 to 1; data on file at Merial

⁶ Opinion Research Corporation, Heartworm Pill Survey, 2009. Data on file at Merial.

⁷ Canine Guidelines: Diagnosis, Prevention and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs. American Heartworm Society web site. Available at: www.heartwormsociety.org/veterinary-resources/canine-guidelines.html. Accessed October 12, 2010.

Heartgard® (ivermectin/pyrantel) Plus

CHEWABLES

CAUTION: Federal (U.S.A.) 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 ascarids (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

DOSAGE: HEARTGARD® Plus (ivermectin/pyrantel) 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 ascarids and hookworms is as follows:

Dog Weight	Chewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older. For dogs over 100 lb 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. 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 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 will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*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 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 ascarids (*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.

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.

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

ADVERSE REACTIONS: In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

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 prevention 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 section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251.



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