

Norbrook®



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April 26, 2007

Dockets Management Branch, HFA-305
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: ANADA Suitability Petition

Dear Sir or Madam:

Enclosed please find, in triplicate, a Suitability Petition submitted in accordance with section 512 (n)(3) of the Federal Food, Drug and Cosmetic Act on behalf of the Sponsor, Norbrook Laboratories Limited, Newry BT35 6PU, Northern Ireland.

The Sponsor requests through this Suitability Petition permission to file an Abbreviated New Animal Drug Application (ANADA) for a generic new animal drug ivermectin/pyrantel pamoate chewable tablet which differs from the pioneer product, Heartguard-30® Plus (ivermectin/pyrantel pamoate) approved under NADA 140-971 (Merial Limited), by the following characteristics: The generic product will be a compressed tablet, whereas the pioneer's product is an extruded tablet.

If you have any questions concerning this petition, please contact me at 913-424-4714.

Sincerely,

Bill Zollers, Ph.D.
Director of Regulatory Affairs – USA & Canada

2007P-0175

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SUITABILITY PETITION

Identification of Petitioner:

Norbrook Laboratories, Ltd
Station Works, Camlough Road
Newry
County Down
Northern Ireland
BT35 6JP

Citation:

Norbrook Laboratories, Ltd submits this petition under section 512 (n) (3) of the Federal Food, Drug, and Cosmetic Act.

Action Requested:

Norbrook Laboratories, Ltd requests permission from the Commissioner to file an Abbreviated New Animal Drug Application (ANADA) for a different dosage form than the pioneer product.

| | |
|---------------------|---------------------------------|
| Pioneer Product: | Heartguard-30 [®] Plus |
| Company: | Merial Limited |
| NADA #: | 140-971 |
| Active Ingredients: | ivermectin/pyrantel pamoate |
| Species: | canine |

The pioneer product is a chewable formulation. It is an extruded product with a texture similar to semi-moist dog food. The proposed generic product will be a chewable compressed tablet. The amount of active ingredients will be the same for both pioneer and generic tablets as will be the dosage of active per pound of body weight. However, the methods of administration will differ in that the dog does not have to be encouraged to chew the tablet. The product will be effective if it is chewed or swallowed whole, due to the dissolution characteristics. A copy of pioneer labeling is enclosed. Both products will indicate that the tablets can be offered by hand or offered in a small amount of dog food.

Statement of Grounds:

The active ingredients of Heartguard-30[®] Plus are ivermectin/pyrantel pamoate formulated as an extruded tablet. The pioneer product is administered orally for the prevention of *Dirofilaria immitis* and the treatment and control of *Toxocara canis*, *Toxascaris leonine*, *Ancylostoma caninum*, and *Uncinaria stenocephala*.

The proposed generic product will have the same indications and dosage, be administered orally, have the same therapeutic effect and contain the same cautions and warnings as the pioneer product. It differs only in the formulation of an extruded chewable tablet for the pioneer as compared to a

compressed chewable tablet for the generic product. The label will differ only as it relates to the different companies manufacturing the two products and the lack of chewing action necessary for the compressed tablet to be effective.

Environmental Impact:

The action of submission and review of this Suitability Petition should not have an impact on the environment. Therefore, Norbrook Laboratories, Ltd requests a categorical exclusion from the requirement to file an environmental assessment as provided under 21 CFR 25.24(a)(8).

Economic Impact:

Norbrook Laboratories, Ltd will provide an economic impact analysis if requested by the Commissioner.

Certification:

Attached is a statement that Norbrook Laboratories, Ltd has included all known unfavorable information regarding this Suitability Petition.

Sincerely,

A handwritten signature in cursive script that reads "Lillian Cromie". The signature is written in black ink and is positioned to the right of the word "Sincerely,".

Dr. Lillian Cromie
Head of Research & Development

CERTIFICATION

The undersigned certifies that no unfavorable information related to this petition has been withheld from the attached Suitability Petition.

Lillian Cromie 16th April 2007
Name Date

Address *Noisbrook Laboratories Limited*
Armagh Road
Newry, Co. Down
BT35 6PU
Northern Ireland.

LABELING

Attached are the pioneer labeling for Heartguard-30[®] Plus and the sections of the label for the Norbrook product which will require revisions.

REVISED LABELING FOR THE NORBROOK PRODUCT

The "Administration" section will read as follows:

"Remove only one tablet at a time from the foil-backed blister card. Return the card with the remaining tablets to its box to protect the product from light. Because the tablets are flavored, the product can be offered to the dog by hand. Alternatively, it may be added to a small amount of food or the dog can be "pilled".

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."

The remainder of the administration section will be unchanged, with the exception of the name of the product.

The "Acceptability" section will be deleted, because palatability will not be claimed. If the dog refuses the tablet, the owner can force swallowing of the whole tablet.

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HEARTGARD® Plus (ivermectin/pyrantel) 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) Chewables 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 | 1 | 68 mcg | 57 mg | Blue |
| 26 - 50 | 1 | 136 mcg | 114 mg | Green |
| 51 - 100 | 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 prevention 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 Chewables were 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 at controlled room temperature of 59°-86°F (15°-30°C). 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, 9 and 12 chewables.

®HEARTGARD is a registered trademark of Merial. © 1998 Merial Limited, Iselin, NJ. 7/98

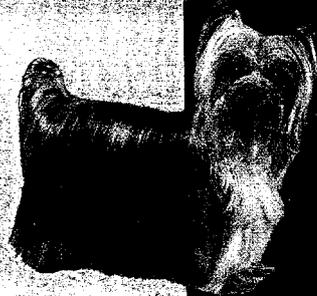
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Heartgard[®] TM

(ivermectin/pyrantel) **Plus**

Administer once a month to prevent heartworm disease and to treat and control ascarid and hookworm infections in dogs.

*For
DOGS
UP TO 25 lbs*



12 Chewables

Each chewable contains 68 mcg ivermectin and 57 mg pyrantel as pamoate salt.

Keep this and all drugs out of the reach of children.

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



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Heartgard[®] 
Plus
(ivermectin/pyrantel)

For DOGS
UP TO 25 lbs.
12 Chewables

9360101

Product **37811**

ENTER DATE ADMINISTERED:



Jan



Feb



Mar



Apr



May



Jun



Jul



Aug



Sep



Oct



Nov



Dec

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

NADA 140-971,
Approved by the FDA.

U.S. Pat. 4,199,569

Marketed by
Merial Limited
3239 Satellite Blvd.
Duluth, GA 30096
Made in USA

HEARTGARD is a registered trademark and Dog & Hand logo is a trademark of Merial.

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Heartgard[®]  TM

(Ivermectin/pyrantel)

Plus

For DOGS
UP TO 25 lbs

12 Chewables

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Heartgard[®] 
(ivermectin/pyrantel) **Plus**

**For DOGS
UP TO 25 LBS**

12 Chewables

7 Lot & Exp

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05-2009**

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Heartgard[®]  **Plus**[™]
(ivermectin/pyrantel)

