



Smart Drug Systems

7 Masons Island Road, Mystic, Connecticut 06355

September 12, 2000

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20857

0430 '00 SEP 15 AM 1:08

To Whom It May Concern:

We are filing this Suitability Petition to request permission to file an ANADA for a generic new animal drug which differs slightly from that of the pioneer product. We wish to file an ANADA to Merial Limited's HEARTGARD® (ivermectin) chewable tablets (NADA 140-886). Whereas the pioneer's product is an extruded chewable tablet, our proposed generic product is a compressed chewable tablet.

1. **PETITIONER:** Smart Drug Systems, Inc.
7 Masons Island Road
Mystic, CT 06355

CITATION: Section 512 (n) (3) of the Federal Food, Drug and Cosmetic Act (the Act).

2. **ACTION REQUESTED:** We request permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product by the following characteristics: Our generic product will be a compressed chewable tablet, whereas the pioneer product is an extruded chewable tablet.
3. **STATEMENT OF GROUNDS:** There are 5 specific variances under the Act for which a Suitability Petition may be submitted. Our petition is for #2 of these variances, change of a dosage form. We are merely changing the dosage form from the pioneer's extruded chewable tablet to our compressed chewable tablet.
4. **ENVIRONMENTAL IMPACT:** Under 21 CFR 25.24 (a) (8) we request a categorical exclusion from the requirement of an environmental

DDP-1519

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assessment because the action of submitting and reviewing this Suitability Petition will not be expected to have an environmental impact.

5. **ECONOMIC IMPACT:** An Economic Impact statement will be provided upon request.
6. **CERTIFICATION:** A separate statement certifying that we have included all information unfavorable to this petition is included in this submission.

Additional essential elements of the petition:

1. **IDENTIFICATION OF DRUG:** The active ingredient in both the pioneer product and our generic is ivermectin. It will be included in our generic product at the same concentration and dosed at the same rate and frequency as the pioneer product.
2. **LABELING FOR THE PROPOSED PRODUCT:** Copies of the proposed labeling for the generic product and approved labeling for the pioneer product are included in this submission. Changes in the generic label indicated in red print. These changes deal with packaging, which has not been determined for the generic product and, as long as it ensures the integrity of the finished product, has no bearing on the actual drug product. Also, in our proposed labeling we are using the generic, active ingredient name, ivermectin, in place of the pioneer's trade name HEARTGARD. Eventually we will have our own trade name, which will replace some of the references to ivermectin.

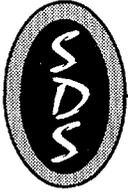
May we have your permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product only in the fact that it is a compressed chewable tablet verses an extruded chewable tablet?

Sincerely,



Jenaay M. Brown DVM
Director, Regulatory Affairs

Attachment



Smart Drug Systems

7 Masons Island Road, Mystic, Connecticut 06355

I do hereby certify that I have included all information unfavorable to this petition;
no unfavorable information has been intentionally withheld from this submission.

Jenaay M. Brown

9/14/00

Jenaay M. Brown DVM
Director, Regulatory Affairs

Date

PROPOSED GENERIC PRODUCT LABEL

IVERMECTIN (ivermectin) Chewables

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

Indication: For use in dogs to prevent canine heartworm disease. IVERMECTIN (ivermectin) prevents heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection.

Dosage: IVERMECTIN Chewables are to be administered orally at the recommended minimum dose level of 6.0 µg of ivermectin per kilogram (2.72 µg/lb.) of body weight at monthly dosing intervals (See **Administration**). The recommended dosage schedule for prevention of canine heartworm disease is as follows:

IVERMECTIN Chewables

<u>Dog Weight</u>	<u>Chewables Per Month</u>	<u>Ivermectin Content</u>	Foil packages not mentioned because generic packaging has not been determined.
Up to 25 lb.	1	68 µg.	
25 to 50 lb.	1	136 µg.	
51 to 100 lb.	1	272 µg.	

For dogs over 100 lbs. Use the appropriate combination of chewables.

IVERMECTIN is recommended for dogs 6 weeks of age and older.

Administration: Remove only one chewable at a time from the packaging. (Foil packages are not mentioned because generic packaging has not been determined) Return the remaining chewables to their box to protect the product from light. Because most dogs find IVERMECTIN Chewables palatable, they can be offered to the dog by hand. Alternatively, they 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 to ensure that the dog consumes the complete dose, and treated dogs should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. For this reason, if the IVERMECTIN chewable is added to dog food, it should be kept intact and not crumbled. If it is suspected that any of the dose has been lost, redosing is recommended. IVERMECTIN 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 after the dog's first exposure to mosquitoes. The final dose must be given within a month after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of IVERMECTIN must be given within a month (30 days) of the last dose of the former medication. If the interval between doses exceeds 30 days, the efficacy of IVERMECTIN can be reduced. Therefore, for optimal performance, IVERMECTIN must be given once a month on or about the same date. If treatment is delayed, whether by a few days or many, immediate treatment with IVERMECTIN and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Efficacy: IVERMECTIN (ivermectin) Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *Dirofilaria immitis* acquired during the previous month (30 days) and, as a result, prevents the development of the adult stage.

Acceptability: In acceptability and field trials IVERMECTIN chewables were shown to be a palatable oral dosage form which will be consumed at the first offering by the majority of dogs.

Safety: IVERMECTIN has shown a wide margin of safety at the recommended dose level in dogs (See Precautions for exceptions) 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 IVERMECTIN chewables in a heartworm disease preventive program.

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. IVERMECTIN demonstrated no signs of toxicity at 10 times the recommended dose (60 µg/kg.) in sensitive Collies. Results of these trials support the safety of IVERMECTIN products in dogs, including Collies, when used as recommended.

Precautions: All dogs should be tested for existing heartworm infections prior to starting treatment with IVERMECTIN, which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae prior to initiating a program with IVERMECTIN.

While some microfilaria may be killed by the ivermectin in IVERMECTIN at the recommended dose level, IVERMECTIN 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 after treatment of some dogs that have circulating microfilaria.

IVERMECTIN Chewables should be stored at controlled room temperature of 59°--86°F (15°--30°C).

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.

Adverse Reactions: The following adverse reactions have been reported following the use of IVERMECTIN: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

How Supplied: IVERMECTIN Chewables are available in three dosage strengths (see dosage section) for dogs of different weights. Each strength comes in convenient dispensers of 6 chewables, packed 10 dispensers per carton.

PIONEER PRODUCT LABEL

HEARTGARD® (ivermectin) Chewables

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HEARTGARD Chewables

<u>Dog Weight</u>	<u>Chewables Per Month</u>	<u>Ivermectin Content</u>	<u>Color coding on Foil Backing and Carton</u>
Up to 25 lb.	1	68 µg.	Blue
25 to 50 lb.	1	136 µg.	Green
51 to 100 lb.	1	272 µg.	Brown

For dogs over 100 lbs. Use the appropriate combination of chewables.

HEARTGARD is recommended for dogs 6 weeks of age and older.

Administration: Remove only one chewable at a time from the foil backed blister card. Return the remaining chewables to their box to protect the product from light. Because most dogs find HEARTGARD Chewables palatable, they can be offered to the dog by hand. Alternatively, they 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.

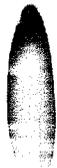
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How Supplied: HEARTGARD Chewables are available in three dosage strengths (see dosage section) for dogs of different weights. Each strength comes in convenient dispensers of 6 chewables, packed 10 dispensers per carton.

HEARTGARD® is a registered trademark of Merial Limited

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