

Headquarters	Fluids	Product Development	Beta Lactams
3915 S. 48th St. Terrace	5915 Corporate Drive	5909 Corporate Drive	2116 8th Avenue South
P.O. Box 8039 (64508)	P.O. Box 8039 (64508)	P.O. Box 8039 (64508)	Fort Dodge, IA 50501
St. Joseph, MO 64503	St. Joseph, MO 64507	St. Joseph, MO 64507	515-576-4225
816-364-3777	816-364-3777	816-364-3777	Fax 515-573-3016
Fax 816-364-3778	Fax 816-671-9965	Fax 816-364-3523	



8884 '02 APR 29 P1:27

Suitability Petition

April 24, 2002

Dockets Management Branch
HFA-305, Room 123
Food and Drug Administration
Park Building
12420 Parklawn Dr.
Rockville, MD 20857

Dear Sir or Madam:

Enclosed is a Suitability Petition submitted in accord with FFDC Section 512 (n) (3) on behalf of Phoenix Scientific, Inc., St. Joseph, MO 64503.

The Petition concerns a change in the physical form of the drug product in a generic Praziquantel Oral Liquid from the approved product, Droncit® (praziquantel) Tablets for oral use in dogs, approved under NADA 111-798, for Bayer Corporation. The requested change is from a compressed tablet for the approved to an oral liquid for the generic.

If there are any questions concerning this petition, or when you have completed your review, please call me at (816) 364-3777.

Sincerely:

Phoenix Scientific, Inc.

Robert D. Gunderson
Vice President, Regulatory Affairs

02P-0189

CPI

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SUITABILITY PETITION

Identification of Petitioner:

This Suitability Petition is submitted on behalf of Phoenix Scientific, Inc., (PSI) 3915 South 48th Street Terrace, St. Joseph, MO 64503 under Section 512 (n) (3) of the Federal Food, Drug, and Cosmetic Act.

Action Requested:

PSI requests permission from the Commissioner to file an Abbreviated New Animal Drug Application (ANADA) consisting of a different physical form of the drug product than the approved product. The approved product, Droncit® (praziquantel) Tablets, 34 mg/tablet (NADA 111-798) is a compressed tablet for oral administration. The proposed generic product will be an oral liquid at 68 mg/m L. The amount of active ingredients administered per dose to the dog will be the same for both products.

The indications for the use of the generic product will be the same as for the approved product. A copy of the approved product labeling is enclosed.

Statement of Grounds:

The proposed product contains the same active ingredient and has the same indications, cautions, and warnings as the approved product. Both products are for oral use in dogs. The products will differ only in the physical form of the drug product, an oral liquid for the generic rather than a compressed oral tablet for the approved product. The label copy will vary only as it relates to the different amount of drug product required to provide the dose. As an example, one (1) mL of the generic oral liquid (68 mg) will equal two (2) approved Droncit® Tablets (2 X 34 mg tablets = 68 mg)

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Environmental Impact:

The action of submitting and reviewing of this Suitability Petition will not normally be expected to have an environmental impact. Therefore, under 21 CFR 25.30(h), we request a categorical exclusion from the requirement to prepare an environmental assessment (EA), since, to the best of our knowledge, no extraordinary circumstances exist as indicated by 21 CFR 25.21.

Economic Impact:

An "Economic Impact" analysis of this action will be provided upon request by the Commissioner.

Certification:

Attached is a statement that Phoenix Scientific, Inc. has included all information known to us, which is unfavorable to this Suitability Petition.

Approval to file an ANADA for this Praziquantel Oral Liquid based upon this Suitability Petition is requested.

Sincerely:

Phoenix Scientific, Inc.


Robert D. Gunderson
Vice President, Regulatory Affairs

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Certificate of Inclusion of Unfavorable Information

As the Vice President of Operations for Phoenix Scientific, Inc., I certify that no unfavorable information related to this Suitability Petition has been withheld from the attached Suitability Petition.

William R. Ellis, Ph.D.
Vice President of Operations
Phoenix Scientific, Inc.
St. Joseph, MO 64503

April 24, 2002

NADA 111-798, Approved by FDA

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

EACH TABLET CONTAINS: 34 mg praziquantel.

DOSAGE AND ADMINISTRATION: Administer orally to dogs as follows:

- 5 pounds and under - 1/2 tablet
- 6-10 pounds - 1 tablet
- 11-15 pounds - 1 1/2 tablets
- 16-30 pounds - 2 tablets
- 31-45 pounds - 3 tablets
- 46-60 pounds - 4 tablets
- Over 60 pounds - 5 tablets max.

Tablets may be given directly or crumbled and offered with the feed. FASTING IS NEITHER NECESSARY NOR RECOMMENDED.

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▲ OPEN AT PERFORATION ▲



130113
JAN 99

Lot No.
Exp. Date

Droncit® (praziquantel)

Canine Cestocide Tablets

Each tablet contains 34 mg praziquantel.

DESCRIPTION: Droncit® (praziquantel) Canine Cestocide Tablets are sized for easy oral administration to either adult dogs or puppies. The tablets may be crumbled and mixed with the feed.

INDICATIONS: Droncit® (praziquantel) Canine Cestocide

Tablets are indicated for the removal of the following canine cestodes: *Dipylidium caninum*, *Taenia pisiformis*, *Echinococcus granulosus* and for the removal and control of *Echinococcus multilocularis*.

ACTION: Droncit® (praziquantel) is absorbed, metabolized in the liver and excreted in the bile. Upon entering the digestive tract from the bile, cestocidal activity is exhibited. Following exposure to praziquantel, the tapeworm loses its ability to resist digestion by the mammalian host.

Because of this, whole tapeworms, including the scolex, are very rarely passed after administration of praziquantel. In many instances only disintegrated and partially digested pieces of tapeworms will be seen in the stool. The majority of tapeworms are digested and are not found in the feces.

USE DIRECTIONS: Droncit® (praziquantel) Canine Cestocide Tablets may be administered directly per os or crumbled and mixed with the feed. The recommended dosage of praziquantel varies according to body weight. Smaller animals require a relatively larger dosage

because of their higher metabolic rate. The optimum dose for each individual animal will be achieved by utilizing the following dosage schedule:

Dogs and Puppies*

5 lbs. and under	1/2 tablet
6-10 lbs.....	1 tablet
11-15 lbs.....	1 1/2 tablets
16-30 lbs.....	2 tablets
31-45 lbs.....	3 tablets
46-60 lbs.....	4 tablets
Over 60 lbs.....	5 tablets max

* Not intended for use in puppies less than 4 weeks of age.

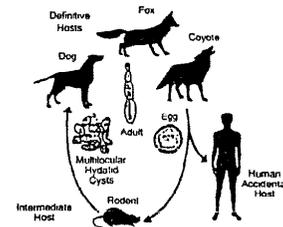
FASTING: The recommended dosage of praziquantel is not affected by the presence or absence of food in the gastrointestinal tract, therefore, **FASTING IS NEITHER NECESSARY NOR RECOMMENDED.**

RETREATMENT: For those animals living where reinfections are likely to occur, clients should be instructed in the steps to optimize prevention, otherwise, retreatment may be necessary. This is true in cases of *Dipylidium caninum* where reinfection is almost certain to occur if fleas are not

removed from the animal and its environment. In addition, for control of *Echinococcus multilocularis*, a program of regular treatment every 21 to 26 days may be indicated (see *E. multilocularis* section below).

ECHINOCOCCUS MULTILOCULARIS: *Echinococcus multilocularis* is a tapeworm species ordinarily considered to be found in wild canids, including foxes, coyotes and wolves. The parasite has also been identified in domestic dogs and cats and potentially is a serious public health concern by involving humans as accidental intermediate hosts.

The life cycle of the parasite is based on a predator-prey relationship, as depicted below.



The adult tapeworm is small (1-4 mm) and resides in the intestinal tract of the definitive host (wild or domestic canids). Eggs from the adult tapeworm are shed in the feces of the infected canid. Rodents such as mice and voles serve as the intermediate host for *E. multilocularis*. Eggs ingested by rodents develop in the liver, lungs and other organs to form multilocular cysts. The life cycle is completed after a canid consumes a rodent infected with cysts. After ingestion of an infected rodent, larvae contained within the cyst develop into adult tapeworms in the intestinal tract of the canid. Eggs may begin to be passed in the feces of

canid approximately 28 days later.

This parasite poses a serious public health problem because of the possibility for human involvement in the life cycle. If eggs shed by an infected canid are accidentally ingested, a highly pathogenic condition (Alveolar Hydatid Disease) results from development of the cyst stage in humans.

The original geographic distribution of *E. multilocularis* was primarily confined to northern areas of North America. Current evidence indicates migration of the parasite well into the continental United States.^{2,3}

Domestic dogs living in *E. multilocularis* endemic areas that

roam freely with the opportunity to catch wild rodents are at risk for infection. Pet owners should be advised on how to minimize this risk. Proper restraint of roaming dogs should be encouraged, along with regular treatment with Droncit tablets, following the established aforementioned dosing schedule and the following precautions.

Additional information on the life cycle and epidemiology of this parasite is available in veterinary parasitology texts.^{4,5}
DIAGNOSIS: Diagnosis of *E. multilocularis* in canids is difficult. The adult tapeworm produces no clinical signs of infection. Tapeworm segments (proglottids) are usually not

observed in the feces. *E. multilocularis* eggs, observed using microscopic fecal examination procedures, are similar in appearance to the common taeniid species of canids such as *Taenia pisiformis*.

Assistance in the diagnosis of *E. multilocularis* may be available from a state veterinary diagnostic laboratory. Additional information regarding areas where *E. multilocularis* is suspected or has been confirmed may be obtained from area veterinary schools or the Centers for Disease Control in Atlanta, GA.

TREATMENT: Dogs infected with *E. multilocularis* should

be treated to prevent exposure of humans to infective eggs and to reduce perpetuation of the parasite's life cycle.

The dosage of Droncit tablets for removal of *E. multilocularis* is the same as that indicated for the removal of the other tapeworm species listed on the label. Laboratory efficacy studies have demonstrated the recommended dosage is 100% efficacious for removal of this tapeworm.

Under condition of continual exposure to wild rodents, retreatment of the dog at 21-26 day intervals is recommended to prevent the shedding of infectious eggs.

PRECAUTIONS: Strict hygienic precautions should be taken

when handling dogs or feces suspected of harboring *E. multilocularis*. Infected dogs treated for the first time with Droncit tablets and dogs treated at intervals greater than 28 days may shed eggs in the feces after treatment. The animal should be held in the clinic during this interval and all feces should be incinerated or autoclaved. If these procedures are not possible, the eggs can be destroyed by soaking the feces in a sodium hypochlorite (bleach) solution of 3.75% or greater.⁶ All areas where the animal was maintained or in contact with should be thoroughly cleaned with sodium hypochlorite and allowed to dry completely

before reuse.

OVERDOSAGE: The safety index has been derived from controlled safety evaluations, clinical trials and prior approved use in foreign countries. Dosages of 5 times the labeled rate at 14 day intervals to dogs as young as 4 weeks did not produce clinical signs of toxicity. No significant clinical chemistry, hematological, cholinesterase, or histopathological changes occurred. Symptoms of gross overdose include vomiting, salivation, diarrhea and depression.

CONTRAINDICATIONS: There are no known contraindications to the use of praziquantel in dogs.

PREGNANCY: Droncit® (praziquantel) has been tested in breeding and pregnant dogs. No adverse effects were noted.

ADVERSE REACTIONS: Seven instances (3.2%) of either vomiting, anorexia, lethargy or diarrhea were reported during the field trials in which 218 dogs were administered Droncit® Canine Cestocide Tablets. The investigators rated these as non-significant.

WARNING: Keep out of the reach of children. Not for human use.

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

HOW SUPPLIED: Bottle of 50, and 150 scored tablets. Each scored tablet contains 34 mg praziquantel.

REFERENCES:

- ¹ Andrews, P., Pharmacokinetic Studies with Droncit® in Animals Using a Biological Assay. *Veterinary Medical Review*, 2/76, pg. 154-165.
- ² Hildreth, M.B., Johnson, M.D. and Kozacos K.R., 1991. A Zoonosis of Increasing Concern in the United States. *Compendium for Cont Ed*, 13(5) 727-740.
- ³ Lieby, P.D., Carney, W.P., and Woods, C.E., 1970. Studies on Sylvatic Echinococcosis. III. Host Occurrence and Geographic Distribution of *Echinococcus multilocularis* in the North Central United States. *J Parasit* 56 (6) 1141-1150.
- ⁴ Georgi, J.R. and Georgi M.E., 1990. *Parasitology for Veterinarians*. W.B. Saunders Co. 118-138
- ⁵ Soulsby, E.J.L., 1982. *Helminths, Arthropods and Protozoa of Domesticated Animals*. 7th Edition. Lea & Febiger. 118-138.

- ⁶ Craig, P.S. and McPharson, C.N.L., 1988 Sodium Hypochlorite as an Ovicide for *Echinococcus*. *Ann Trop Med and Parasit* 82 (2) 211-213.

Droncit is a registered TM of the parent company of Bayer AG, Leverkusen.

Product Code 1828 — 50 Tablets
Code 1860 — 150 Tablets
Made in U.S.A.

NADA 111-798, Approved by FDA

Bayer 

Bayer Corporation, Agriculture Division,
Animal Health
Shawnee Mission, Kansas 66201 U.S.A.

June, 1995