

Date of Approval: MAR 25 2003

FREEDOM OF INFORMATION SUMMARY

Abbreviated New Animal Drug Application

ANADA 200-350

Exodus™ (pyrantel pamoate) Paste

Pyrantel pamoate paste is indicated for the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

Sponsor:

Cross Vetpharm Group Limited
Tallaght, Dublin, Ireland

1. GENERAL INFORMATION:

- a. ANADA Number: 200-350
- b. Sponsor: Cross Vetpharm Group Limited
Tallaght, Dublin, Ireland
- c. Established Name: Pyrantel Pamoate Oral Paste
- d. Proprietary Name: Exodus™ (pyrantel pamoate) Paste
- e. Dosage Form: Oral Paste
- f. How supplied: 23.6 gm syringes containing the equivalent of 3.6 gm of pyrantel base (171 mg pyrantel base as pyrantel pamoate per mL of paste)
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: 3.6 grams of pyrantel base in 23.6 g (171 mg pyrantel base as pyrantel pamoate per mL) of paste.
- i. Route of Administration: Oral, via pre-filled syringe, adjustable to body weight by 300 pound increments.
- j. Species: Equine
- k. Recommended Dosage: The dose rate is 3 milligrams pyrantel base per pound of body weight.
- l. Pharmacological Category: parasiticide/anthelmintic
- m. Indications for use: Pyrantel pamoate paste is indicated for the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

- n. Pioneer Product: Strongid[®] (pyrantel pamoate) Paste, Pfizer Animal Health, NADA 129-831.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act, (53 FR 50460, December 15, 1988; First GADPTRA Policy Letter), an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). The sponsor has demonstrated *in vivo* bioequivalence, via clinical endpoint bioequivalence studies, of the generic product to the pioneer product to support safety and efficacy of the generic product.

Clinical endpoint bioequivalence studies were considered appropriate for pyrantel pamoate paste for horses because it is locally active in the intestinal tract, poorly absorbed into the circulatory system, and blood levels have not been shown to be reflective of clinical effectiveness. The parasite species selected for the studies below are among those labeled species more resistant to the effects of pyrantel. It is believed that bioequivalence demonstrated against these parasite species provides evidence to support the bioequivalence of the generic product for all claims found on the labeling.

Two clinical endpoint bioequivalence studies to assess the *in vivo* bioequivalence of Cross Vetpharm's formulation of pyrantel pamoate 43.9% paste, Exodus[™] Paste (test product) in horses compared to Pfizer's Strongid[®] Paste (reference product) when administered at the recommended dosage were conducted. The studies are summarized below. The investigator for both studies was:

Craig R. Reinemeyer, D.V.M.
East Tennessee Clinical Research, Inc.
Knoxville, Tennessee 37921

a. Study One Summary and Results

Thirty adult male and female horses with natural infections of *Cylicocyclus nassatus*, *Strongylus edentatus* and other large strongyle species were randomly assigned to three groups containing 10 animals each for a total of thirty (30) test subjects. The study was conducted as a single period design in which one group received the test product, Exodus[™] Paste and the second received the pioneer product, Strongid[®] Paste, and the third group received a placebo. All products were administered according to label directions.

Fourteen (14) days later, the horses were euthanized and measured samples of the gut contents were collected.

The study was completed May 1998 through August 1998. No adverse effects attributable to the medications given were seen.

The individual worm counts were made and “percent efficacy” was calculated for the groups administered the generic, pioneer, and control products. The only parasite for which efficacy calculations could be determined was *Cylicocyclus nassatus*, a small strongyle. Both the pioneer and the generic products demonstrated greater than 90 % efficacy and were considered bioequivalent. Another parasite (*Strongylus edentatus*) was found in numbers too small for a valid determination of efficacy to be established.

Nematode	Quantitative Parameter	Exodus	Strongid	Controls
<i>Cylicocyclus nassatus</i>	Geometric Mean	289.3	342.6	3847.2
	Percent Efficacy	92.5%	91.1%	(N/A)

The geometric mean numbers of adult *Cylicocyclus nassatus* for the generic and the pioneer products were each significantly less ($p < 0.01$) than the placebo control group. The parasite burden was adequate. Percent efficacy against *C. nassatus* was greater than 90% and thus no further analysis was undertaken. The parasite burden for *Strongylus edentatus* was too low to establish significance in the study.

Conclusion

The test product, Exodus™ Paste was found to be bioequivalent to the Reference Product, Strongid® Paste with respect to claims for efficacy against *C. nassatus*, a small strongyle species.

b. Study Two Summary and Results

Thirty-six male and female horses, of mixed breeds, from 6 months to 20 years of age (34/36 horses were < 20 months of age), with natural infections of *Parascaris equorum* were randomly assigned to three groups containing 12 animals each for a total of thirty (36) test subjects. One group received the test product, Exodus™ Paste, another received the pioneer product, Strongid® Paste, and the third group received a placebo. All products were administered

according to label directions. Horses were observed once or twice daily to assess their health status. Ten to eleven (10 to 11) days later, the horses were euthanized and measured samples of the gut contents were collected for parasite counting and identification. Blinding during the study was accomplished through separation of function by the study employees. Those employees responsible for making observations and collecting data were unaware of the treatments given to the horses. The study was completed from March 2001 to May 2001. No adverse effects attributable to the medications given were noted.

The only parasite present in adequate numbers for evaluation was *Parascaris equorum*. The individual worm counts were made and "percent efficacy" was calculated for the groups administered the generic, pioneer, and control products. Both the pioneer and the generic product demonstrated greater than 90 % efficacy against *Parascaris equorum* and were considered bioequivalent.

Nematode	Quantitative Parameter	Test	Reference	Controls
<i>Parascaris equorum</i>	Geometric Mean	1.14	0.95	37.04
	Percent Efficacy	96.9%	97.4%	N/A

Adult *Parascaris equorum* geometric mean counts for the generic and pioneer groups were significantly less ($p < 0.001$) than the placebo control group. The parasite burden was adequate. Percent efficacy against these nematodes was greater than 90% and no further analysis was undertaken.

Conclusion

The test product, Exodus™ Paste was found to be bioequivalent to the Reference Product, Strongid® Paste with respect to the claim for efficacy against *Parascaris equorum*.

3. HUMAN SAFETY:

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this ANADA. The drug is approved for use only in horses that are not to be used for food and is labeled:

"WARNING: NOT FOR USE IN HORSES INTENDED FOR FOOD."

HUMAN SAFETY RELATIVE TO POSSESSION, HANDLING, AND ADMINISTRATION

The product labeling contains adequate caution/warning statements.

4. AGENCY CONCLUSIONS:

This is an Abbreviated New Animal Drug Application (ANADA) filed under section 512(b)(2) of the Federal, Food, Drug and Cosmetic (FFD&C) Act.

Safety and effectiveness for this generic animal drug, Exodus™ Paste, were established by the demonstration of clinical end-point bioequivalence to the pioneer product, Strongid Paste®, NADA 129-831.

This generic product and the pioneer product have identical labeling indications for use in horses. The marketing status, and, route and method of administration, of the two drugs are identical. Both drugs are administered orally. The generic and pioneer products contain the same active ingredient in the same concentration.

This ANADA satisfies the requirements of section 512(n) of the Act and demonstrates that Exodus™ Paste is safe and effective for its labeled indications, when used under the proposed conditions of use.

5. ATTACHMENTS:**a. Generic Labeling:**

Syringe label
Carton label
Display carton label
Shipper carton label

b. Pioneer Labeling:

Package Insert
Syringe label
Carton label

Syringe Label
8PYR002 23.6 g

NDC 61133-0141-0

Exodus™

(pyrantel pamoate) Paste
Equine Anthelmintic

Net Wt.
23.6 g

▶ **WARNING: NOT FOR USE IN HORSES INTENDED FOR FOOD** ◀
KEEP OUT OF REACH OF CHILDREN

Active Ingredients: Each syringe contains 3.6 grams pyrantel base in 23.6 grams paste
FOR ANIMAL USE ONLY FOR ORAL USE ONLY ANADA # XXX-XXX Approved by FDA
INDICATIONS FOR USE: For the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*), small strongyles, pinworms (*Oxyuris equi*), and large roundworms (*Parascaris equorum*) in horses and ponies

DOSAGE: Exodus™ Paste (pyrantel pamoate) is to be administered as a single oral dose of 3 milligrams pyrantel base per pound of body weight. The syringe has four weight mark increments. Each weight mark indicates the recommended dose for 300 pounds of body weight.

Body Weight Range	Quantity	mg Pyrantel Base
up to 300 lb	1/4 syringe	900 mg
301 to 600 lb	1/2 syringe	1800 mg
601 to 900 lb	3/4 syringe	2700 mg
901 to 1200 lb	1 full syringe	3600 mg

NOTE: Position ring-gauge over appropriate mark on plunger.
It is recommended that severely debilitated animals not be treated with this preparation.

CAUTION: CONSULT YOUR VETERINARIAN FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT AND CONTROL OF PARASITISM.

RECOMMENDED STORAGE:
STORE AT 15-30°C (59°-86°F)

REFER TO CARTON FOR COMPLETE DIRECTIONS

TAKE TIME



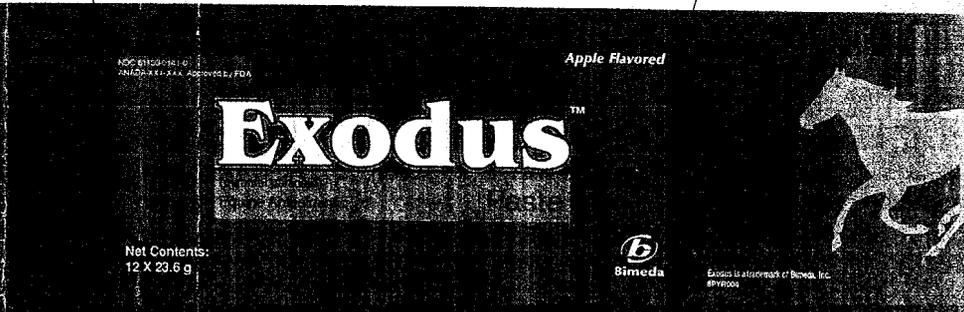
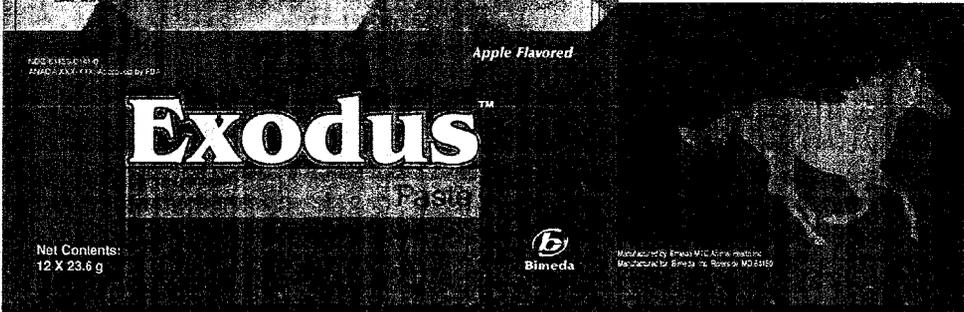
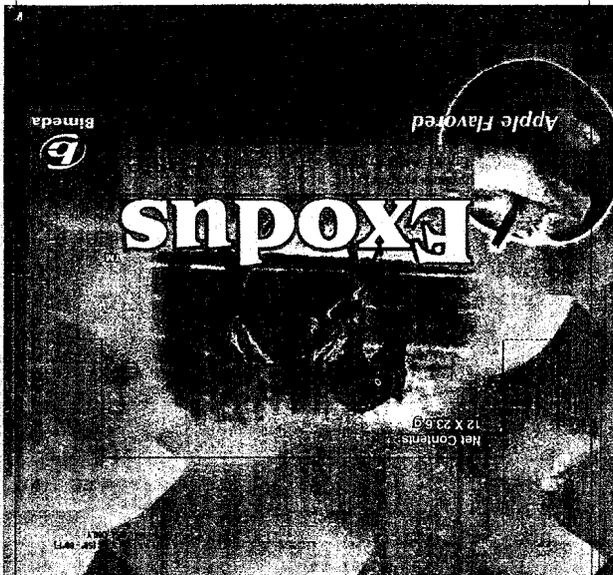
OBSERVE LABEL DIRECTIONS



Manufactured by
Bimeda-MTC Animal Health Inc.
Manufactured for
Bimeda, Inc.
Riverside, MO 64150
TM Bimeda Inc.

8PYR002 Lot
Exp

Overlap area. Not Varnished



Exodus™ Paste

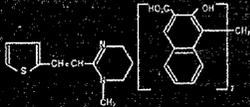
(pyrantel pamoate)
Equine Anthelmintic
ANADA #XXX-XXX, Approved By FDA

Exodus™ Paste (pyrantel pamoate) is a pale yellow to buff paste containing 43.9% w/w pyrantel pamoate in an inert vehicle. Each syringe contains 3.6 grams pyrantel base in 23.6 grams paste. Each milliliter contains 171 milligrams pyrantel base as pyrantel pamoate.

READ ENTIRE CARTON CAREFULLY BEFORE USING THIS PRODUCT

COMPOSITION

Pyrantel pamoate is a compound belonging to a family classified chemically as tetrahydropyrimidines. It is a yellow, water-insoluble crystalline salt of the tetrahydropyrimidine base and pamoic acid containing 34.7% base activity. The chemical structure and name are given below.



Chemical Name: (E)-1,4,5,6-tetrahydro-1-methyl-2-[2-(2-thienyl)-vinyl]-pyrimidine 4,4'-methylenebis[3-hydroxy-2-naphthoate] (1:1)

INDICATIONS

For the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*), small strongyles, pinworms (*Oxyuris equi*), and large roundworms (*Parescaus equorum*) in horses and ponies.

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

DOSAGE AND TREATMENT

Exodus™ Paste (pyrantel pamoate) is to be administered as a single oral dose of 3 milligrams pyrantel base per pound of body weight. The syringe has four weight mark increments. Each weight mark indicates the recommended dose for 300 pounds of body weight.

DOSAGE

Body Weight Range	Quantity	mg Pyrantel Base
up to 300 lb	1/4 syringe	800 mg
301 to 600 lb	1/2 syringe	1600 mg
601 to 900 lb	3/4 syringe	2400 mg
901 to 1200 lb	1 full syringe	3600 mg

NOTE: Position ring-gauge over appropriate mark on plunger.

8PYR003

UPC CODE 80%

For maximum control of parasitism, it is recommended that foals (2-8 months of age) be dosed every 4 weeks. To minimize the potential source of infection that the mare may pose to the foal, the mare should be treated 1 month prior to anticipated foaling date followed by re-treatment 10 days to 2 weeks after birth of foal. Horses and ponies over 8 months of age should be routinely dosed every 6 weeks.

It is recommended that severely debilitated animals not be treated with this preparation.

ADMINISTRATION

After removing the cap, the paste should be deposited on the dorsum of the tongue. Introduce the nozzle end of the syringe at the corner of the mouth. Direct the syringe backwards and depress the plunger to deposit the paste onto the tongue. Given in this manner, it is unlikely that rejection of the paste will occur. Raising the horse's head sometimes assists in the swallowing process. When only part of the paste has been used, replace the cap on the syringe nozzle.

EFFICACY

Critical (worm count) studies in horses demonstrated that pyrantel pamoate administered at the recommended dosage was efficacious against mature infections of *Strongylus vulgaris* (>90%), *S. edentatus* (86%), *S. equinus* (>90%), *Oxyuris equi* (81%), *Parescaus equorum* (>90%), and small strongyles (>90%).

WARNING:
NOT FOR USE IN HORSES INTENDED FOR FOOD
KEEP THIS AND ALL MEDICATIONS OUT OF REACH OF CHILDREN
FOR ORAL USE ONLY
FOR ANIMAL USE ONLY

STORAGE: Store at 15-30°C (59-86°F).

MANUFACTURED BY

Bimeda
Manufactured by
Bimeda, LLC
Bimeda, LLC
Florence, MO 63113

Exodus is a Bimeda
® Bimeda, LLC

Exodus™ Paste

(pyrantel pamoate)
Equine Anthelmintic

NADA 61133-01-11-0
ANADA# XXX-XXX, Approved by FDA

Net Contents: 23.6 g

Exodus™ Paste

(pyrantel pamoate)

Apple Flavored

Bimeda

Exodus™
(pyrantel pamoate) Paste
Equine Anthelmintic

10/21/03/02

STRONGID® PASTE

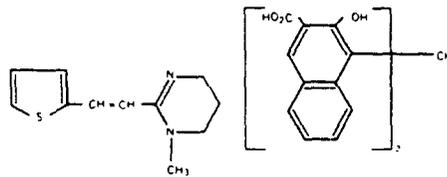
(pyrantel pamoate)
Equine Anthelmintic
NADA #129-831, Approved By FDA

STRONGID® PASTE is a pale yellow to buff paste containing 43.9% w/w pyrantel pamoate in an inert vehicle. Each syringe contains 3.6 grams pyrantel base in 23.6 grams (20 ml) paste. Each milliliter contains 180 milligrams pyrantel base as pyrantel pamoate.

READ ENTIRE BROCHURE CAREFULLY
BEFORE USING THIS PRODUCT

COMPOSITION

Pyrantel pamoate is a compound belonging to a family classified chemically as tetrahydropyrimidines. It is a yellow, water-insoluble crystalline salt of the tetrahydropyrimidine base and pamoic acid containing 34.7% base activity. The chemical structure and name are given below.



Chemical Name: (E)-1,4,5,6-tetrahydro-1-methyl-2-[2-(2-thienyl)-vinyl]-pyrimidine
4,4'-methylenebis[3-hydroxy-2-naphthoate] (1:1)

INDICATIONS FOR USE

For the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*), small strongyles, pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

DOSAGE AND TREATMENT

STRONGID® PASTE is to be administered as a single oral dose of 3 milligrams pyrantel base per pound of body weight. The syringe has four weight mark increments. Each weight mark indicates the recommended dose for 300 pounds of body weight.

Body Weight Range	DOSAGE	
	Volume	mg Pyrantel Base
up to 300 lb	1/4 syringe (5 ml)	900 mg
301 to 600 lb	1/2 syringe (10 ml)	1800 mg
601 to 900 lb	3/4 syringe (15 ml)	2700 mg
901 to 1200 lb	1 full syringe (20 ml)	3600 mg

NOTE: Position screw-gauge over appropriate mark on plunger. Each milliliter contains 180 milligrams pyrantel base as pyrantel pamoate.

For maximum control of parasitism, it is recommended that foals (2-8 months of age) be dosed every 4 weeks. To minimize the potential source of infection that the mare may pose to the foal, the mare should be treated 1 month prior to anticipated foaling date followed by re-treatment 10 days to 2 weeks after birth of foal. Horses and ponies over 8 months of age should be routinely dosed every 6 weeks.

ADMINISTRATION

After removing the cap, the paste should be deposited on the dorsum of the tongue. Introduce the nozzle end of the syringe at the corner of the mouth. Direct the syringe backwards and depress the plunger to deposit the paste onto the tongue. Given in this manner, it is unlikely that rejection of the paste will occur. Raising the horse's head sometimes assists in the swallowing process. When only part of the paste has been used, replace the cap on the syringe nozzle.

EFFICACY

Critical (worm count) studies in horses demonstrated that STRONGID® PASTE (pyrantel pamoate) administered at the recommended dosage was efficacious against mature infections of *Strongylus vulgaris* (>90%), *S. edentatus* (69%), *S. equinus* (>90%), *Oxyuris equi* (81%), *Parascaris equorum* (>90%), and small strongyles (>90%).

▲ **WARNING: NOT FOR USE IN HORSES INTENDED FOR FOOD**
KEEP OUT OF REACH OF CHILDREN ▲

It is recommended that severely debilitated animals not be treated with this preparation.

RECOMMENDED STORAGE: STORE AT ROOM TEMPERATURE, 15°-30°C (59°-86°F)



Distributed by

Animal Health

Division of Pfizer Inc, NY, NY 10017

Made in Canada
23-4345-00-2
12112-11-2

Issued May 1993

Strongid® Paste

(pyrantel pamoate)

1156

pfizer

Equine Anthelmintic

Active Ingredients: Each 20 milliliter syringe contains
3.6 grams pyrantel base in 23.6 grams of paste
FOR ANIMAL USE ONLY
FOR ORAL USE ONLY
NADA #129-831, Approved by FDA

Net Contents: 20 mL (23.6g)

INDICATIONS FOR USE: For the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

DOSAGE: Administer as a single oral dose of 3 milligrams pyrantel base per pound of body weight. The syringe has four weight mark increments. Each weight mark indicates the recommended dose for 300 pounds of body weight.

Body Weight Range	Volume	mg Pyrantel Base
up to 300 lb	1/4 syringe (5 mL)	900 mg
301 to 600 lb	1/2 syringe (10 mL)	1800 mg
601 to 900 lb	3/4 syringe (15 mL)	2700 mg
901 to 1200 lb	1 full syringe (20 mL)	3600 mg

NOTE: Position screw-gauge over appropriate mark on plunger. Each milliliter contains 180 milligrams pyrantel base as pyrantel pamoate. It is recommended that severely debilitated animals not be treated with this preparation.

WARNING:
NOT FOR USE IN HORSES INTENDED FOR FOOD
KEEP OUT OF REACH OF CHILDREN
CAUTION: CONSULT YOUR VETERINARIAN FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT, AND CONTROL OF PARASITISM.
RECOMMENDED STORAGE: STORE AT ROOM TEMPERATURE, 59°-86°F (15°-30°C)
REFER TO PACKAGE INSERT FOR COMPLETE USE DIRECTIONS

Distributed by

Pfizer Animal Health
Division of Pfizer Inc., NY, NY 10017

TAKE TIME



OBSERVE LABEL DIRECTIONS

LOT NO

EXP

MADE IN CANADA

C84488

09/01

1212 05 1

44445-00 1

10-4345-00-2
12112-14-2

DOSSAGE: Administer as a single oral dose of 3 milligrams pyrantel base per pound of body weight. The syringe has four weight mark increments. Each weight mark indicates the recommended dose for 300 pounds of body weight.

Body Weight Range	Volume	mg Pyrantel Base
up to 300 lb	1/4 syringe (5 mL)	900 mg
301 to 600 lb	1/2 syringe (10 mL)	1800 mg
601 to 900 lb	3/4 syringe (15 mL)	2700 mg
901 to 1200 lb	1 full syringe (20 mL)	3600 mg

NOTE: Position screw-gauge over appropriate mark on plunger. Each milliliter contains 180 milligrams pyrantel base as pyrantel pamoate.

For maximum control of parasitism, it is recommended that foals (2-8 months of age) be dosed every 4 weeks. To minimize the potential source of infection that the mare may pose to the foal, the mare should be treated 1 month prior to anticipated foaling date followed by re-treatment 10 days to 2 weeks after birth of foal. Horses and ponies over 8 months of age should be routinely dosed every 6 weeks.

It is recommended that severely debilitated animals not be treated with this preparation.

Strongid[®] Paste
(pyrantel pamoate)



Strongid[®] Paste

1156

(pyrantel pamoate)

Equine Anthelmintic

Net Wt 20 mL(23.6 g)

NADA #129-831, Approved by FDA

The safe and effective horse and foal dewormer that is easy to use

Each 20 milliliter syringe contains 3.6 grams pyrantel base in 23.6 grams of paste.

Strongid[®] Paste
(pyrantel pamoate)

Equine Anthelmintic



588

REFER TO PACKAGE INSERT FOR COMPLETE USE DIRECTIONS

WARNING: NOT FOR USE IN HORSES INTENDED FOR FOOD

KEEP OUT OF REACH OF CHILDREN

FOR ANIMAL USE ONLY

FOR ORAL USE ONLY

CATION: CONSULT YOUR VETERINARIAN FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT, AND CONTROL OF PARASITISM

RECOMMENDED STORAGE: STORE AT ROOM TEMPERATURE, 59 - 86 F (15 - 30 C) MADE IN CANADA

INDICATIONS FOR USE: For the removal and control of mature infections of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

PROOF OF PURCHASE

1156

Pfizer Animal Health
Division of Pfizer Inc. NY, NY 10017



9

TAKE TIME OBSERVE LABEL DIRECTIONS

pfizer
Strongid[®] Paste
(pyrantel pamoate)
Equine Anthelmintic