

HFA-305

Date of Approval MAY 14 2003

FREEDOM OF INFORMATION SUMMARY

Original New Animal Drug Application

NADA 141-216

Quest[®] Plus (moxidectin/praziquantel) Gel

Fort Dodge Animal Health

For the treatment and control of gastrointestinal parasites of horses and ponies six months of age and older.

NADA 141-216

FOIS

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FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number: NADA 141-216
- b. Sponsor: Fort Dodge Animal Health
Division of Wyeth
800 Fifth Street, NW
Fort Dodge, IA 50501

Drug Labeler Code: 000856
- c. Established Names: Moxidectin and praziquantel
- d. Proprietary Name: Quest Plus (moxidectin/praziquantel) Gel
- e. Dosage Form: Oral
- f. How Supplied: Packaged in ready-to-use Sure-Dial[®] syringe. Each syringe contains 0.4 oz. (11.6 g) Quest Plus Gel which is adequate to treat one horse with a body weight of up to 1250 lb, or multiple horses and ponies with combined body weights of 1250 lb.
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: Contains 20 mg moxidectin/mL (2.0% w/v) and 125 mg praziquantel/mL (12.5% w/v).
- i. Route of Administration: Oral
- j. Species/Class: Equine
- k. Recommended Dosage: 0.4 mg moxidectin/kg and 2.5 mg praziquantel/kg (2.2 lb) body weight
- l. Pharmacological Category: Anthelmintic
- m. Indications: Quest Plus Gel is indicated for the treatment and control of the following stages of gastrointestinal parasites of horses and ponies:

Large strongyles

Strongylus vulgaris – (adult and L₄/L₅ arterial stages)

Strongylus edentatus – (adult and tissue stages)

Triodontophorus brevicauda – (adults)

Triodontophorus serratus – (adults)

Small strongyles

Cyathostomum spp. – (adults)

Cyathostomum catinatum – (adults)

Cylicocycclus spp. – (adults)

Cylicostephanus spp. – (adults)

Gyalocephalus capitatus – (adults)

Undifferentiated luminal larvae

Encysted cyathostomes

Late L₃ and L₄ mucosal cyathostome larvae

Ascarids

Parascaris equorum – (adults and L₄ larval stages)

Pinworms

Oxyuris equi - (adults and L₄ larval stages)

Hairworms

Trichostrongylus axei - (adults)

Large-mouth stomach worms

Habronema muscae - (adults)

Horse stomach bots

Gasterophilus intestinalis - 2nd and 3rd instars

Gasterophilus nasalis - 3rd instars

Tapeworms

Anoplocephala perfoliata – (adults)

One dose suppresses strongyle egg production for 84 days.

2. EFFECTIVENESS:

a. Dosage Characterization:

Moxidectin is approved under NADA 141-087 for oral use in horses and ponies at a dose rate of 0.4 mg/kg (2.2 lb) body weight. This dose level of moxidectin was selected for Quest Plus Gel. Studies demonstrating effectiveness against all parasites listed in the Quest Plus Gel indications, except for adult *Cyathostomum catinatum* and *Anoplocephala perfoliata*, at the recommended 0.4 mg/kg body weight dose level are described in the July 11, 1997 and October 4, 1999 NADA 141-087 Freedom of Information Summaries.

Praziquantel was included in this combination drug for cestodocidal activity. Published data indicate greater than 95% effectiveness for the removal of *Anoplocephala perfoliata* with single oral treatments of experimental formulations providing between 1 and 2 mg praziquantel/kg body weight (see Little, SE: *Compend. Contin. Educ. Pract. Vet* 21:356-360, 1999). Other published data from an experiment conducted outside the U.S. indicate that 2.5 mg/kg praziquantel is 100% effective against *Anoplocephala perfoliata*. This experiment studied an overseas commercial combination anthelmintic for equine use that includes praziquantel administered at a dose rate of 2.5 mg/kg body weight (see Tancedi, IP, *et al.*: *Revista Brasileiro de Parasitologia Veterinaria*, 6:256, 1997). On this basis, Quest Plus Gel was formulated to deliver 2.5 mg praziquantel/kg body weight in a single oral dose.

b. Substantial Evidence:

A series of non-interference, dose-confirmation and field studies were conducted to evaluate the effectiveness of Quest Plus Gel when administered to horses and ponies as a single oral dose at the recommended rate of 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight. The final Quest Plus Gel formulation was used in these studies. For evaluation of effectiveness in these studies, *Gasterophilus intestinalis* (bots) was the dose-limiting parasite for moxidectin and *Anoplocephala perfoliata* was the dose-limiting parasite for praziquantel.

(1) Non-Interference/Dose Confirmation Study No. 0696-E-US-2-99

Title: Dose Confirmation and Noninterference Trial of a Combination Formulation of 2% Moxidectin Equine Oral Gel and 12.5% Praziquantel Against the Horse Bot *Gasterophilus intestinalis*, and Equine Tapeworms, *Anoplocephala* spp., in Tennessee

Type of Study: Non-Interference/Dose-Confirmation Study

Investigator: Craig R. Reinemeyer, DVM, PhD
East Tennessee Clinical Research, Inc.
Knoxville, Tennessee 37909

Purpose: The objectives of this study were to determine if either moxidectin or praziquantel interfere with the effectiveness of Quest Plus Gel against the dose-limiting species for each of the active ingredients and provide confirmation of the effectiveness of the recommended dose level of Quest Plus Gel against each of the dose-limiting species.

Animals: A total of 32 horses at least nine months of age weighing between 590-1160 lb with naturally-acquired equine tapeworm and horse stomach bot infections.

Control: Placebo-treated with gel vehicle in oral syringe

Dosage Form: Final Quest Plus Gel formulation in oral syringe

Route of Administration: Oral

Dosage Groups: (8 horses per group)

Each test horse received a single dose of one of the following treatments:

- Control group placebo-treated with gel vehicle formulation containing 0 mg moxidectin and 0 mg praziquantel/kg body weight in Sure-Dial syringe.
- Gel vehicle formulation containing 0.0 mg moxidectin and 2.5 mg praziquantel/kg body weight.
- Gel vehicle formulation containing 0.4 mg moxidectin and 0.0 mg praziquantel/kg body weight.
- Final Quest Plus Gel formulation at recommended dose level of 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight.

Test Duration: 14 days

Pertinent Measurements/Observations: The presence of naturally-acquired horse stomach bot (*Gasterophilus intestinalis*) and equine tapeworm (*Anoplocephala* spp.) infections was demonstrated by gastroscopy and fecal evaluation, respectively, as a condition for inclusion in the study. Test animals were observed for general health at approximately 3 and 24 hours posttreatment and then daily for the duration of the study. Approximately two weeks following treatment, the test horses were sacrificed, necropsied and parasites present in the gastrointestinal tract were collected.

Results:

- (a) Parasite recovery data and percent effectiveness calculated using geometric means for *Anoplocephala perfoliata* are provided in the table below.

Table 1. Summary of *A. perfoliata* data by treatment group

Treatment Group	No. Infected Horses	Geometric Mean	Effectiveness (%)
Controls	8/8	42.7	n/a
Moxidectin	8/8	54.6	0.0
Praziquantel	1/8	0.1	99.8*
Quest Plus Gel	0/8	0.0	100.0*

*Significant treatment effect (P<0.05) compared to control

(b) Parasite recovery data and percent effectiveness calculated using geometric means for *Gasterophilus intestinalis* (2nd and 3rd instars) are furnished in the tables below.

Table 2. Summary of *G. intestinalis* 2nd instar data by treatment group

Treatment Group	No. Infected Horses	Geometric Mean	Effectiveness (%)
Control	8/8	44.7	n/a
Moxidectin	6/8	1.8	95.9*
Praziquantel	7/8	27.4	38.7
Quest Plus Gel	7/8	2.3	94.9*

*Significant treatment effect (P<0.05) compared to control

Table 3. Summary of *G. intestinalis* 3rd instar data by treatment group

Treatment Group	No. Infected Horses	Geometric Mean	Effectiveness (%)
Control	8/8	23.4	n/a
Moxidectin	2/8	0.5	97.7*
Praziquantel	7/8	12.2	47.8
Quest Plus Gel	3/8	1.1	95.5*

*Significant treatment effect (P<0.05) compared to control

(c) Parasite recovery data and percent effectiveness calculated using geometric means for *Cyathostomum catinatum*, a species for which moxidectin effectiveness has not been previously demonstrated, are furnished in the table below.

Table 4. Summary of *Cyathostomum catinatum* data by treatment group

Treatment Group	No. Infected Horses	Geometric Mean	Effectiveness (%)
Control	6/8	756.8	n/a
Moxidectin	0/8	0.0	100.0*
Praziquantel	7/8	2977.5	0.0
Quest Plus Gel	0/8	0.0	100.0*

*Significant treatment effect (P<0.05) compared to control

(d) The gel was readily accepted by all the treated horses and no health abnormalities attributable to treatment with Quest Plus Gel were observed in any of the test horses.

Conclusions:

- (a) Non-interference – Tapeworms: No interference with cestodicidal activity was observed when praziquantel was combined with moxidectin in the final Quest Plus Gel formulation.
- (b) Effectiveness – Tapeworms: The recommended dose level of the final Quest Plus Gel formulation was 100% effective against *Anoplocephala perfoliata*.
- (c) Non-interference – Bots: No interference with boticidal activity was observed when moxidectin was combined with praziquantel in the final Quest Plus Gel formulation.
- (d) Effectiveness – Bots: The recommended dose level of the final Quest Plus Gel formulation was 94.9% and 95.5% effective against the 2nd and 3rd instar stages of *G. intestinalis*, respectively.
- (e) Effectiveness – *Cyathostomum catinatum*: The recommended dose level of the final Quest Plus Gel formulation was 100% effective against this specific small strongyle species.

(2) Dose-Confirmation Study No. 0696-E-US-06-00

Title: Dose Confirmation Trial of a Combination Formulation of 2% Moxidectin Equine Oral Gel and 12.5% Praziquantel Against the Horse Bot, *Gasterophilus intestinalis*, and *Anoplocephala* spp. Tapeworms, in Louisiana

Type of Study: Dose-Confirmation Study

Clinical Investigator: Thomas Klei, Ph.D.
Louisiana State University
Baton Rouge, Louisiana 70803

Purpose: The objective of this study was to confirm that the recommended 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight dose of the final Quest Plus Gel formulation is effective against the dose-limiting species for moxidectin and praziquantel.

Animals: A total of 16 mixed-breed horses between 1-18 years of age and 298-640 lb body weight with naturally-acquired equine tapeworm and horse stomach bot infections.

Control: Untreated

Dosage Form: Final Quest Plus Gel formulation in syringe

Route of Administration: Oral

Dosage Groups: (8 horses per group)

Each test horse received a single dose of one of the following treatments:

- The control horses were not treated.
- Final Quest Plus Gel formulation at recommended dose level of 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight.

Test Duration: 14 days

Pertinent Measurements/Observations: The presence of naturally-acquired horse stomach bot (*Gasterophilus intestinalis*) and equine tapeworm (*Anoplocephala* spp.) infections was demonstrated by gastroscopy and fecal evaluation, respectively, as a condition for inclusion in the study. Test animals were observed for general health at approximately 3 and 24 hours posttreatment and then daily for the duration of the study. Approximately two weeks following treatment, the test horses were sacrificed, necropsied and parasites present in the gastrointestinal tract were collected.

Results:

(a) Parasite recovery data and percent effectiveness calculated using geometric means for the dose-limiting species for moxidectin (*Gasterophilus intestinalis*) and praziquantel (*Anoplocephala perfoliata*) are provided in the table below.

Table 5. Dose Confirmation: Dose-limiting Parasites

Parasite Species	No. Infected Controls	Geometric Mean Data		Effectiveness (%)
		Control	Quest Plus Gel	
<i>G. intestinalis</i> (2 nd instars)	6/8	5.2	0.1*	98.3
<i>G. intestinalis</i> (3 rd instars)	8/8	70.1	2.7*	96.1
<i>Anoplocephala perfoliata</i>	8/8	94.5	0.00*	100.0

*Significant treatment effect (P<0.05) compared to control

(b) Parasite recovery data and percent effectiveness calculated using geometric means for adult *Cyathostomum catinatum*, a species for which moxidectin effectiveness has not been previously demonstrated, are furnished in the table below.

Table 6. Dose Confirmation: *Cyathostomum catinatum* (adults)

Parasite Species	No. Infected Controls	Geometric Mean Data		Effectiveness (%)
		Control	Quest Plus Gel	
<i>C. catinatum</i> (adults)	7/8	1901.9	0.0*	100.0

*Significant treatment effect (P<0.05) compared to control

(c) The gel was readily accepted by all the treated horses and no health abnormalities attributable to treatment with Quest Plus Gel were observed in any of the test horses.

Conclusion: Data collected in this study confirms that the recommended 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight dose rate of the final Quest Plus Gel formulation is effective against the dose-limiting species for each of the active components of the combination. The recommended dose level of the final Quest Plus

Gel formulation was also shown to be 100% efficacious against *Cyathostomum catinatum* in this study

(3) Field Studies

A multi-center effectiveness field study was conducted in separate geographic locations in the U.S. This study furnished data pertaining to both the effectiveness and safety of Quest Plus Gel under field use conditions. A combined summary of these four trials is presented below.

Type of Study: Effectiveness Field Study

Investigators & Locations:

Study No. 0696-E-US-09-01

Dr. Thomas Yazwinski
University of Arkansas
Fayetteville, Arkansas

Study No. 0696-E-US-10-01

Dr. Douglas Hutchens
University of Illinois
Urbana, Illinois

Study No. 0696-E-US-11-01

Dr. Larry Smith
Larry Smith R & D
Lodi, Wisconsin

Study No. 0696-E-US-12-01

Dr. Craig Reinemeyer
East Tennessee Clinical Research
Knoxville, Tennessee

Purpose: The purpose of these studies was to evaluate the safety and effectiveness of the recommended dose level of Quest Plus Gel (0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight) when administered under field conditions.

Animals: A total of 400 client-owned equine stock ranging in age from four months to 31 years and ranging in weight from 211 to 1450 pounds completed this series of field studies. The study population included various breeds of horses, ponies, and miniature horses.

Dosage Groups

- Control group: 100 test animals were administered gel vehicle formulation containing 0 mg moxidectin and 0 mg praziquantel/kg body weight in a Sure-Dial syringe.
- Treated group: 300 test animals were given final Quest Plus Gel formulation containing the recommended dose level of 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight in a Sure-Dial syringe.

Route of Administration: Oral

Test Duration: Single administration with 14-day posttreatment observation period with the exception of one farm in Tennessee that performed the last posttreatment health

observation on Day 16 posttreatment. The follow-up period was extended in the Illinois study to 42 days posttreatment in order to do additional fecal sampling.

Study Design: At each geographic location, 100 client-owned horses over four months of age were enrolled in the study with no restrictions on sex or breed. Pregnant mares and breeding stallions were excluded from these trials. For masking purposes, the test animals were randomly assigned to one of four treatment groups. Three of the treatment groups were given the recommended level of Quest Plus Gel. The fourth group was treated with identically-appearing syringes containing blank gel vehicle formulation. The owners and individuals treating and making health observations were not aware of the treatment being administered. The treated horses and ponies were observed for signs of adverse reactions for a 14-day posttreatment period.

Pertinent Measurements/Observations: Prior to treatment, all test animals were given a complete physical examination. Initial health observations were made approximately 4 and 8 hours posttreatment. Additional follow-up observations were made on Days 1, 2, 7 and 14 posttreatment. Fecal samples were taken for fecal egg count determination prior to treatment and again at the end of the 14-day posttreatment observation period. At the Illinois sites, additional fecal sampling was accomplished on Days 28/29 and 42.

Results: All strongyle egg counts were transformed to the natural logarithm (count+1) which was used to calculate the geometric means at each site. Percent reduction was calculated using the formula: $[C-T] / C \times 100$, where C = the geometric mean of the control group and T = the geometric mean of the treated group.

Strongyles

At all four sites, a reduction of strongyle egg counts was demonstrated, when compared to the control, of >98% with a p value of <0.05 using 1-sided Student's t-test.

Cestodes

The following table is a compilation of the cestode data:

Table 7. Cestode Data

Pre-Treatment Cestode Status	Treatment	No. (n)	Post-Treatment Cestode Status	
			Negative	Positive
Positive	Untreated Control	20	6 (30%)	14 (70%)
	Combination Drug	72	69 (96%)	3 (4%)

Fisher's exact test, $p < 0.0001$

There were no signs of adverse reaction observed in any of the 300 treated and 100 control horses and foals that participated in these four field trials.

Conclusion: Under field conditions, a single oral Quest Plus Gel treatment at the recommended 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight dose level was safe and effectively reduced strongyle and *Anoplocephala* spp. fecal egg counts in a wide variety (in terms of age, sex and breed) of horses and ponies.

3. TARGET ANIMAL SAFETY:

Two experiments were conducted to evaluate the safety of Quest Plus Gel when administered to young horses and ponies as a single oral dose at the recommended dose level of 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight. The final Quest Plus Gel formulation was used in this animal safety testing program.

a. Drug Tolerance Test - Study No. 0696-E-US-04-00

Title: "Tolerance of Single Administration of Moxidectin/Praziquantel Oral Equine Gel Given Once to Young Horses"

Type of Study: Laboratory Safety Study

Investigator: Charles E. Heird, Ph.D.
Southwest Bio-Labs, Inc.
Las Cruces, New Mexico 88005

Purpose: The objective of this study was to evaluate the safety of the final moxidectin/praziquantel equine oral gel formulation in groups of foals and young horses given single treatments containing either 5X or 6X the recommended dose level.

Animals: Eight young horses approximately 6½–8½ months of age and eight foals approximately 3–5½ months old participated in this study. These two age groups of test animals weighed between 428 to 532 lb (194 to 241 kg), and 126 to 406 lb (57 to 184 kg), respectively.

Control: Sham-treated with an empty syringe

Dosage Form: Final Quest Plus Gel formulation in syringe

Route of Administration: Oral

Dosage Groups:

<u>Treatment Set¹</u>	<u>Age Group²</u>	<u>Treatment Level</u>	<u>AM or PM Treatment</u>
A	Yearlings (2)	5X (Sham)	AM
	Yearlings (2)	5X (Drug)	AM
B	Yearlings (2)	6X (Sham)	PM
	Yearlings (2)	6X (Drug)	PM
C	Foals (2)	5X (Sham)	AM
	Foals (2)	5X (Drug)	AM
D	Foals (2)	5X (Sham)	PM
	Foals (2)	5X (Drug)	PM

¹Treatment set consists of 2 control and 2 treated test animals of same age group

²Yearling = 6½–8½ months age group; foals = 3– 5½ months old group

Test Duration: 7 days.

Pertinent Measurements/Observations: Test animals were observed at least twice daily (AM and PM) for general health. For animals treated in the morning (AM), additional observations were made at 1, 2, 4, 6, 8, 10, and 14 hours posttreatment on Day 0. For animals treated in the evening (PM), additional observations were made on Day 0 at 1, 2, and 5 hours posttreatment, then on Day 1 at approximately 14, 16, 18, 20, and 22 hours posttreatment. Each animal received a physical examination, including blood and urine collection pretreatment, approximately 24 hours posttreatment and on Day 7. Physical examinations without blood or urine collection were performed on Days 2 and 3. Individual animal food consumption was recorded starting at least 7 days prior to treatment. Blood was collected and analyzed three times pretreatment and on Days 1 and 7 posttreatment. Urine samples were collected three times pretreatment and on Days 1 and 7 posttreatment.

Results:

(1) **Clinical Observations:** Two of the four foals that received a 5X dose did not show any signs of adverse reaction to treatment. The signs seen in the other two 5X foals included ataxia, incoordination, lethargy, depression and droopy lips and eyelids. These signs were seen in the first 5X foal at 14 hours posttreatment. This foal was normal by the 24-hour observation point. The onset of signs in the second 5X foal was 24 hours posttreatment, returning to normal by the 48-hour observation. One of the two 5X yearlings showed the same signs listed above at 23 hours posttreatment and had returned to normal by the 48-hour observation. Both yearlings that received the 6X dose showed the same signs listed above. The onset of signs in both animals was 14 hours posttreatment. Both animals had returned to normal by the 24-hour observation.

- (2) **Feed Consumption:** Feed intake remained relatively consistent throughout the treatment period for all test animals, with the exception of one 6X yearling which was noted to have lower daily average consumption.
- (3) **Hematology, Coagulation, Serum Chemistry:** There were no treatment-related findings in hematology, coagulation, or clinical chemistry data.
- (4) **Urinalysis:** No effect of treatment was seen in the urine parameters.

Conclusion: The animal health observations reported in this study characterize the adverse effects resulting from the administration of exaggerated doses (5X and 6X the recommended dose rate) of the final Quest Plus Gel formulation to foals and young horses. The signs attributed to these high levels of the drug were ataxia, incoordination, lethargy, depression and droopy lip and eyelids. The onset of signs in this study was 14 or more hours posttreatment. All animals returned to normal by 48 hours posttreatment.

b. Target Animal Toxicity Study – Study No. 0696-E-US-08-01

Title: Target Animal Safety Study (Toxicity) in Foals Approximately 4 Months Old Treated with Moxidectin/Praziquantel Oral Equine Gel

Type of Study: Laboratory Safety Study

Study Director: Charles E. Heird, Ph.D.
Southwest Bio-Labs, Inc.
Las Cruces, New Mexico, 88005

Purpose: The objective of this study was to evaluate the clinical and pathological effects when the final Quest Plus Gel formulation was administered to approximately 4 month old foals given three times at weekly intervals at either 1X, 3X, or 4X the recommended dose level.

Animals: Thirty-two foals (16 males and 16 females) approximately 3 to 5 months of age weighing between 194-412 lb.

Control: Sham-treated with an empty syringe

Dosage Form: Final Quest Plus Gel formulation in syringe

Route of Administration: Oral

Dosage Groups: (8 foals per group)

Each test foal received one of the following treatments once weekly for three weeks:

- Controls sham-treated with an empty syringe (corresponding to a 4X dose level)
- 0.4 mg moxidectin and 2.5 mg praziquantel/kg body weight (recommended dose level)
- 1.2 mg moxidectin and 7.5 mg praziquantel/kg body weight (3X recommended dose level)
- 1.6 mg moxidectin and 10.0 mg praziquantel/kg body weight (4X recommended dose level)

Test Duration: 30-32 days

Pertinent Measurements/Observations: A minimum of twice-daily health observations were made during the trial. In addition, observations were made approximately 1, 2, and 4 hours after the evening treatments (given on Days 0, 7, and 14). Observations were also made on the day following treatment at approximately 14, 16, 18, 20, and 22 hours posttreatment. Physical exams were performed at 12 hours and at 24 hours posttreatment. In addition, body weights, physical examinations, food consumption, and blood analyses were evaluated weekly. Urinalysis was done pretreatment, following the third treatment, and prior to necropsy. Animals were necropsied in the 5th week after the 1st treatment. All animals were examined for gross pathology at necropsy. Tissues from the control and high dose (4X) treatment groups were examined microscopically.

Results:**(1) Clinical Observations:** No reactions were noted in the control (0X) group.

Slight lethargy and ataxia were reported in one foal following the first 1X dose. A single observation of slight ataxia was noted in this same foal following administration of the second 1X dose. Slight lethargy was observed in one other foal following the first 1X dose. No reactions were recorded for this foal following subsequent 1X treatments. The reactions were first noted in the 1X Group at approximately 14 to 18 hours posttreatment and dissipated within a period of two to six hours. There were no reports of animals in the 1X Group reacting after the third treatment.

Transient signs of adverse reaction to treatments (slight depression, slight ataxia, and/or droopy lips) were reported in some of the animals receiving the 3X and 4X treatments. In general, reactions were first noted at approximately 16 to 18 hours posttreatment (range 14–20 hours). The last recorded reactions were noted between 18–26 hours posttreatment with one exception. One 4X foal was observed to be slightly ataxic at 39 hours after the third dose. This animal returned to normal by 45 hours posttreatment. In general, the test foals showing these signs took longer to return to normal after the second and third treatments.

(2) Feed Consumption: There were no statistically significant differences between treatment groups.

- (3) **Body Weight:** There were no statistically significant differences between treatment groups. Body weights increased over time for all animals as expected for growing foals.
- (4) **Hematology, Coagulation, Serum Chemistry, and Urinalysis:** A comparison of pre- and posttreatment hematology, coagulation, clinical chemistry, and urinalysis values indicated no biologically significant changes.
- (5) **Pathology Observations:** No gross lesions suggestive of treatment-related toxicity were observed at necropsy. Similarly, microscopic evaluation of all major tissues obtained from test animals in the high-dose (4X) group at necropsy revealed no histopathologic changes indicative of a toxic effect.

Conclusion: Under the conditions of this study, 12 of the foals treated with the final Quest Plus Gel formulation showed transient signs including slight depression, slight ataxia, and/or droopy lips. All affected test foals returned to normal without intervention or significant long-term health effects. No other clinical or pathological effects were noted in any of the treated foals. Based on this outcome, especially noting lethargy and/or ataxia in two of the 1X foals, the minimum age for use of this product was determined to be 6 months.

4. HUMAN SAFETY:

This drug is intended for use in horses and ponies, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this NADA.

Human Warnings are provided on the product label as follows: "Not for human use. Keep this and all other drugs out of the reach of children. Do not ingest. If swallowed, induce vomiting. Wash hands and contaminated skin with soap and water. If accidental contact with eyes occurs, flush repeatedly with water. If irritation or any other symptom attributable to exposure to this product persists, consult your physician."

5. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR 514 of the implementing regulations. The data demonstrate that Quest Plus Gel, when administered as a single oral dose containing 0.4 mg moxidectin/kg and 2.5 mg praziquantel/kg body weight is safe and effective for the treatment of the equine gastrointestinal parasites specified on the product label.

Quest Plus Gel is labeled for OTC use. Routine deworming of horses is a widely accepted and recommended practice performed by the lay person. A diagnosis of parasite infection prior to deworming is not necessary.

Under section 512(c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval.

Moxidectin is under the following U.S. patent numbers:

U.S. Patent Number
4,916,154

Date of Expiration
April 10, 2007

6. ATTACHMENTS:

Package Insert

Syringe Label

Printed Outer Carton

7520A

NADA 141-216, Approved by FDA

FORT DODGE

QUEST PLUS^{GEL}

moxidectin / praziquantel



QUEST PLUS Oral Gel

Contains 20 mg moxidectin/mL (2.0% w/v)
and 125 mg praziquantel/mL (12.5% w/v)

DEWORMER & BOTICIDE

**FOR ORAL USE IN HORSES AND
PONIES SIX MONTHS OF AGE AND
OLDER**

INDICATIONS

QUEST PLUS (moxidectin/praziquantel) Equine Oral Gel when administered at the recommended dose level of 0.4 mg moxidectin/kg and 2.5 mg praziquantel/kg (2.2 lb) body weight is effective in the treatment and control of the following stages of gastrointestinal parasites in horses and ponies:

Large strongyles

Strongylus vulgaris – (adults and L₁/L₂ arterial stages)
Strongylus edentatus – (adults and tissue stages)
Triodontophorus brevicauda – (adults)
Triodontophorus serratus – (adults)

Small strongyles

Cyathostomum spp. – (adults)
Cyathostomum californicum – (adults)
Cylococtus spp. – (adults)
Cylococtophanus spp. – (adults)
Gyaloccephalus capitatus – (adults)
Undifferentiated luminal larvae

Encysted cyathostomes

Late L₃ and L₄ mucosal cyathostome larvae

Ascarids

Parascaris equorum – (adults and L₄ larval stages)

Pinworms

Oxyuris equi – (adults and L₄ larval stages)

Hairworms

Trichostrongylus axei – (adults)

Large-mouth stomach worms

Habronema muscae – (adults)

Horse stomach bots

Gasterophilus intestinalis – (2nd and 3rd instars)
Gasterophilus nasalis – (3rd instars)

Tapeworms

Anoplocephala perfoliata – (adults)

One administration of the recommended dose rate of QUEST PLUS (moxidectin/praziquantel) Equine Oral Gel also suppresses strongyle egg production through 84 days.

STRATEGIC PROTECTION PROGRAMS

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. For best control of parasites, all horses and ponies should be included in a strategic treatment program, with particular attention given to high performance animals. In foals, initial treatment is recommended at 6 months of age, after which they should be included in a recurrent treatment program. Because QUEST PLUS provides effective control of the mucosal stages of small strongyles (encysted cyathostomes) and tapeworms, it is useful in reducing the frequency of treatment required for successful strategic equine parasite control. A veterinarian can assist in preparing the best program for your needs.

QUEST PLUS Equine Oral Gel when used at the recommended dose rate suppresses strongyle egg production through 84 days following a single oral administration. This residual strongyle control reduces pasture contamination and provides a period of protection from reinfection for horses and ponies maintained on the same pasture.

MODE OF ACTION

QUEST PLUS Equine Oral Gel contains two active pharmaceutical ingredients, moxidectin and praziquantel. Moxidectin acts by interfering with chloride channel-mediated neurotransmission in the parasite. This results in paralysis and elimination of the parasite. Moxidectin is safe for use in horses and ponies because it does not have the same injurious effect on the mammalian nervous system. Praziquantel increases the tapeworm's membrane permeability to calcium and other cations causing severe contraction and paralysis of the tapeworm's muscles. This spastic paralysis results in the inability of tapeworms to attach to the host's intestinal wall. Detached tapeworms are either destroyed by the host's immune defense system or passed in the feces.

(continued on opposite side)

ADMINISTRATION AND DOSAGE

QUEST PLUS (moxidectin/praziquantel) Equine Oral Gel is specially formulated as a palatable gel which is easily administered to horses and ponies. QUEST PLUS Gel is packaged in ready-to-use SURE-DIAL® syringes (see diagram of the SURE-DIAL® syringe below). The syringe is calibrated in 50-pound increments, up to 1250 pounds. This enables the administration of the recommended dose level by choosing a setting consistent with the animal's weight.

HOW TO SET THE DOSE

Since the dose is based on the weight of the animal, you need to use a scale or weight tape to find each animal's weight before treating with QUEST PLUS Gel. Once the weight is known, set the dose for each horse or pony as follows.

1. Hold the syringe with the capped end pointing to the left and so that you can see the weight measurements and tick marks (small black lines) as shown in the diagram below. Each tick mark relates to 50 lbs. of body weight.
2. Turn the green dial ring until the left side of the ring lines up with the weight of the animal. In the diagram below, the dial ring is set to dose a 500 lb. animal.

HOW TO GIVE QUEST PLUS GEL TO A HORSE OR PONY

1. Make sure there is no feed in the animal's mouth.
2. Remove the cap from the end of the syringe. Save the cap for reuse.
3. Place the tip of the syringe inside the animal's mouth at the space between the teeth.
4. Gently push the plunger until it stops, depositing the gel on the back of the tongue.
5. Remove the syringe from the animal's mouth and raise the animal's head slightly to make sure it swallows the gel.
6. Replace the syringe cap.

ANIMAL SAFETY

QUEST PLUS (moxidectin/praziquantel) Equine Oral Gel can be safely administered at the recommended dose to horses and ponies of all breeds at least 6 months of age and older. Transient ataxia, incoordination, lethargy, depression and droopy lips and eyelids may be seen when very young or debilitated animals are treated. In these instances, supportive care may be advisable. Reproductive studies evaluating the safety of QUEST PLUS in mares at or near the time of breeding, pregnant mares and breeding stallions have not been conducted.

To report adverse drug reactions or to obtain a copy of the Material Safety Data Sheet (MSDS) call (800)477-1365.

ENVIRONMENTAL SAFETY

Care should be taken to avoid the release of significant volumes of this product into either ground or free-running water since moxidectin may be injurious to aquatic life. SURE-DIAL® syringes and their contents should be disposed of in an approved landfill or by incineration.

PRECAUTIONS

QUEST PLUS Equine Oral Gel has been formulated specifically for use in horses and ponies only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

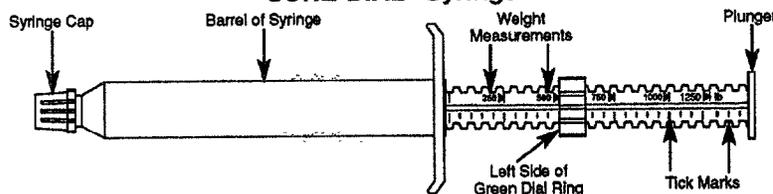
WARNINGS

Extreme caution should be used when administering the product to foals, young and miniature horses, as overdosage may result in serious adverse reactions. Do not use in sick, debilitated, or underweight animals. Do not use in horses or ponies intended for food.

HUMAN WARNINGS

Not for use in humans. Keep this and all drugs out of the reach of children. Do not ingest. If swallowed, induce vomiting. Wash hands and contaminated skin with soap and water. If accidental contact with eyes occurs, flush repeatedly with water. If irritation or any other symptom attributable to exposure to this product persists, consult your physician.

SURE-DIAL® Syringe



TREATING A SECOND HORSE OR PONY WITH THE SAME SYRINGE

If the first animal you treat weighs less than 1250 lbs., there will be gel left in the syringe. You can use this gel to treat other horses or ponies. To set the next dose, add the weight of the animal you want to treat to the dose setting already on the syringe. For example, if the syringe was first used to treat a 250 lb. animal, the green dial ring is set to 250 lbs. To treat a 500 lb. animal next, move the green dial ring to the 750 lb. marking (250+500=750). You need more than one syringe to treat horses weighing more than 1250 lbs.

Each syringe of QUEST PLUS Equine Oral Gel may be used to treat more than one animal especially when dosing ponies and growing and lighter breeds of horses. The table below will help estimate the number of horses or ponies the contents of each syringe will treat.

Age	Ponies			Light Horses			Heavy Horses		
	Weight (lbs)	(kg)	Treated Animals (per syringe)	Weight (lbs)	(kg)	Treated Animals (per syringe)	Weight (lbs)	(kg)	Treated Animals (per syringe)
6 months	200	(91)	6	400	(181)	3	550	(250)	2
9 months	250	(113)	5	500	(227)	2	700	(318)	1
Mature	450	(204)	2	900	(409)	1	1300	(590)	1

* A full syringe plus a portion of a second syringe is required to treat horses weighing more than 1250 lb.

HOW SUPPLIED

QUEST PLUS Equine Oral Gel is available in one syringe applicator size. Each SURE-DIAL® syringe contains 0.4 oz (11.8 g) of QUEST PLUS Equine Oral Gel which is sufficient to treat a single horse weighing up to 1250 lb, or two or more lighter animals with a combined body weight of up to 1250 lb.

NDC 0856-7521-01 — 0.4 oz (11.8 g) syringe - 20 mg moxidectin and 125 mg praziquantel per mL

Store at or below 77°F (25°C). Avoid freezing. If frozen, thaw completely before use. Store partially-used syringes with the cap tightly secured.

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Fort Dodge, Iowa 50501 USA

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QUEST[®] PLUS_{GEL}

moxidectin/praziquantel

Equine Oral Gel

Contains 20 mg moxidectin/mL (2.0% w/v)
and 125 mg praziquantel/mL (12.5% w/v)
0.4 oz (11.6 g) gel

HORSE DEWORMER & BOTICIDE

NDC 0946-7521-01 FOR ORAL USE IN HORSES AND PONIES SIX MONTHS OF AGE AND OLDER
ADMINISTRATION AND DOSAGE: Each syringe treats a single horse weighing up to 1250 lb. or two or more lighter animals with a combined body weight of up to 1250 lb. Please read entire insert for ADMINISTRATION AND DOSAGE and other important information.
WARNINGS: Extreme caution should be used when administering the product to foals, young and infirm horses, as overdosage may result in serious adverse reactions. Do not use in sick, debilitated, or underweight animals. Do not use in horses or ponies intended for food.
HUMAN WARNINGS: Not for use in humans. Keep this and all drugs out of the reach of children. Do not ingest. If swallowed, induce vomiting. Wash hands and contaminated skin with soap and water. If accidental contact with eyes occurs, flush repeatedly with water. If irritation or any other symptoms attributable to exposure to this product persists, consult your physician.
PRECAUTIONS: Quest Plus (moxidectin/praziquantel) Oral Gel has been formulated specifically for use in horses and ponies only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
STORAGE: Store at or below 77°F (25°C). Avoid freezing. If frozen, thaw completely before use. Store partially-used syringe with the cap tightly secured.
NADA 141-216, Approved by FDA. U.S. Patent No. 4,916,154



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