

Approval Date: JUN 1 2006

FREEDOM OF INFORMATION SUMMARY

**ORIGINAL ABBREVIATED NEW ANIMAL
DRUG APPLICATION**

ANADA 200-391

**Griseofulvin Powder Microsize
(Griseofulvin)**

For the treatment of ringworm infection in horses

Sponsored by:

IVX Animal Health, Inc.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number ANADA 200-391
- b. Sponsor: IVX Animal Health, Inc.
3915 South 48th Street Ter.
St. Joseph, MO 64503

Drug Labeler Code: 059130
- c. Established Name: Griseofulvin
- d. Proprietary Name: Griseofulvin Powder Microsize
- e. Dosage Form: Powder
- f. How Supplied: 15-gram tubes and
15-gram pouches
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: 2.5 grams Griseofulvin (microsize)
- i. Route of Administration: Oral
- j. Species/Class: Horses
- k. Recommended Dosage: Adults – 2 packet or bottle per day
(2.5 grams).
Yearlings – ½ to 1 packet or bottle per
Day (1.25-2.5 grams).
Foals - ½ packet or bottle per
day.
- l. Pharmacological Category: Antifungal, antibiotic
- m. Indications: Equine – Ringworm infection caused by
Trichophyton equinum or *Microsporum*
gypseum.
- n. Pioneer Product: FULVICIN U/F (Griseofulvin microsize)
Powder; NADA 39-792; Schering-Plough
Animal Health Corp.

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 (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

<http://www.fda.gov/cvm/guidance/published.htm#documents>

Based on the formulation characteristics of the generic product, IVX Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product Griseofulvin Powder Microsize. The generic product is administered as an oral solution, contains the same active ingredients in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product, FULVICIN U/F (Griseofulvin microsize) Powder, the subject of Schering-Plough Animal Health Corp. NADA 39-792, was approved on May 19, 1970.

3. HUMAN SAFETY:

This drug is intended for use in horses, 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 ANADA.

Human Warnings are not provided on the product label.

4. AGENCY CONCLUSIONS:

This supplemental ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that Griseofulvin Powder Microsize, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-391:

Label 15 gram bottle

Label 15 gram pouch

Package Insert

Pioneer Labeling for NADA 39-792:

15 gram pouch

Carton of 50 15-gram packets

Package Insert

For oral administration to horses – not for use in horses intended for food. The powder may be given on a small amount of feed or in a drench.

Usual Dose: One half to one bottle daily.

TAKE TIME
 OBSERVE LABEL DIRECTIONS

Manufactured by IVX Animal Health, Inc.
Fort Dodge, IA 50501
AmTech® is a registered trademark of IVX Animal Health, Inc.

Lot No.

Exp. Date

NDC 59130-767-83

Griseofulvin Powder Microsize Veterinary

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

ANADA 200-381. Approved by FDA

NET WEIGHT: 15 grams

Contains 2.5 g Active Ingredient



Indication: Equine ringworm infection caused by *Trichophyton equinum* or *Microsporum gypseum*.

Read accompanying directions carefully.

Store between 2° and 30°C
(36° and 86°F)

780504

T-1es1105



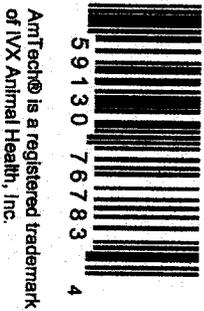
3 59130 76783 4

Griseofulvin Powder

Microsize

For oral administration to horses—not for use in horses intended for food.
The powder may be given on a small amount of feed or in a drench.
Indication: Equine ringworm infection caused by *Trichophyton equinum*
or *Microsporum gypseum*.
Usual Dose: One half to one packet daily.
Store between 2° and 30°C (36° and 86°F).
Read accompanying directions carefully.

780504
T-15a1105
Manufactured by
VX Animal Health, Inc.
Fort Dodge, IA 50501



AmTech® is a registered trademark
of VX Animal Health, Inc.

Lot No.

Exp. Date



NDC 59130-767-83

Griseofulvin Powder

Microsize
Veterinary

Caution: Federal law restricts this drug to use by
or on the order of a licensed veterinarian.

ANADA 200-391, Approved by FDA

NET WEIGHT: 15 Grams

Contains 2.5 g Active Ingredient

AmTech®
Group, Inc.

ANADA 200-391, Approved by FDA

Griseofulvin Powder (microsize)

Veterinary
For Oral Use In Horses

CAUTION Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION Griseofulvin Powder (microsize) is available in 15-gram packets and 15-gram bottles each containing 2.5 grams griseofulvin (microsize). Griseofulvin Powder (microsize) is an orally effective antifungal antibiotic specifically active against superficial fungi which cause tinea (ringworm) of the skin and hair. This microsize form of griseofulvin differs from regular Griseofulvin Powder products in that its finer particle size results in a much greater surface area for absorption. An increased blood level has been obtained in experimental studies in man using fine particle size griseofulvin, indicating better absorption and a greater amount of the drug available for fungistatic action in the skin and hair.

GENERAL CONSIDERATIONS In human medicine, Griseofulvin Powder (microsize) is indicated in the treatment of infections caused by dermatophytic fungi of the skin, hair, and nails. Of those organisms which cause these conditions, the following are responsive to oral therapy with Griseofulvin Powder (microsize): *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Trichophyton schoenleinii*, *Trichophyton sulphureum*, *Trichophyton verrucosum*, *Trichophyton interdigitale*, *Epidermophyton floccosum*, *Microsporium gypseum*, *Microsporium canis*, *Microsporium audouini*. Griseofulvin Powder (microsize) is inactive against bacteria and yeasts including *Monilia*, *Actinomyces*, *Nocardia*, *Blastomyces*, *Coccidioides*, *Histoplasma*, *Cryptococcus*, *Sporotrichum*, and *Aspergillus*.

The Griseofulvin Powder (microsize) product is administered orally until the fungi have been eliminated from the skin and hair. The length of therapy will vary with the severity of the infection. The time necessary for the

newly formed, fungal-resistant keratin to reach the surface varies greatly with different structures, such as hair and thin body skin. Experimental and clinical work indicates that animals showing involvement of skin and hair only may require treatment for 3 to 4 weeks. Cure is considered complete when repeated cultures are negative for the presence of fungi. In the absence of these tests, therapy should be continued until lesions are clinically improved and there is evidence of resumed hair growth.

The infected skin in many cases shows a remarkably rapid improvement, with decreased itching and inflammation occurring in a few days. In some cases the skin may appear normal clinically in as short a time as 10 days. Viable fungi in the outer layers may persist, however, and the possibility of reinfection is not known with certainty. The optimal period of treatment has not yet been determined. Clipping of the hair to help remove any remaining viable fungi is indicated. Hair that is clipped from the infected lesion should be burned.

INDICATIONS Equine - Ringworm infection caused by *Trichophyton equinum* and *Microsporium gypseum*.

Adults - 1 packet or bottle per day (2.5 grams).

Yearlings - 1/2 to 1 packet or bottle per day (1.25-2.5 grams).

Foals - 1/2 packet or bottle per day.

Cases of ringworm in horses caused by *T. equinum* and *M. gypseum* should be treated with the Griseofulvin Powder (microsize) product for a period of not less than 10 days. Responsive cases may show clinical signs of recovery in 5 to 7 days after griseofulvin therapy is initiated. In responsive cases, treatment should be continued until all infected areas are negative by appropriate culture.

If cases do not respond to therapy in 3 weeks, it is recommended that the diagnosis be reevaluated.

The powder may be given on a small amount of feed or in a drench.

Not for use in horses intended for food.

WARNING The safety and efficacy of prophylactic use of griseofulvin has not been established. This drug should not be used to treat minor or trivial infections.

Safety of griseofulvin for use in pregnant animals has not been established. It has been reported in the Soviet literature (N.N. Slonitskaya; Teratogenic Effect of Griseofulvin-Forte on the Rat Fetus/Antibiotiki 14(1): 44-48, 1969) that a griseofulvin preparation was found to be embryotoxic and teratogenic on oral administration to pregnant Wistar rats. In addition, pups and kittens with either cleft palates or other abnormalities have been reported in litters of bitches and queens treated with griseofulvin during gestation.

PRECAUTIONS Patients on prolonged therapy with any potent medication should be under close observation. Periodic monitoring of organ system function, including renal, hepatic, and hemopoietic, should be done.

This antibiotic is derived from a species of *Penicillium griseofulvum*. A number of known penicillin-sensitive humans have been treated with griseofulvin without difficulty. In veterinary medicine, the drug apparently has no allergenic properties; however, considerably more experience in this area must be obtained before definite conclusions may be drawn.

Griseofulvin administered to animals intraperitoneally or intravenously in massive doses will produce damage to the seminal epithelium; however, no such effects have been observed following oral administration of usual clinical doses to dogs and cats.

Studies to date indicate that the usual clinical doses of griseofulvin administered orally have no effect on spermatogenesis. More evidence is needed, but it appears likely that such effects noted are related to the massive doses administered by the parenteral routes. The effects of griseofulvin on stallion spermatogenesis are not known.

SIDE EFFECTS Close observation of human and animal patients receiving therapeutic doses thus far reveals no effect on body weight, fasting blood sugar, blood electrolytes, total or differential counts, thymol turbidity tests, urinalyses, or sternal marrow counts.

In the human, heartburn, nausea, epigastric discomfort, and diarrhea have occasionally been reported. In a

few instances, urticaria or drug rashes have developed and in these instances the drug should be withdrawn. Generally, the incidence of side effects has been quite low and the drug seems to be well tolerated when given orally.

The veterinarian is alerted to the following griseofulvin-associated side effects which have been reported in either human or veterinary literature: irritability, dizziness, memory loss, visual disturbances, antagonism to barbiturates and other drugs metabolized by the liver, such as warfarin-type anticoagulants.

It has also been reported that griseofulvin effects disturbances in porphyrin metabolism, formation of hepatomata and cocarcinogenicity with methylcholanthrene; also higher fat diet increases absorption of the antibiotic.

GENERAL MEASURES Clearing of dermatophytic infections with oral griseofulvin therapy is a great advance. However, it is necessary to maintain general hygienic precautions. The possibility of recurrence is not known. Destruction of old bedding, disinfection of stall, a close clipping of hair just before termination of therapy, etc., are measures which should reduce incidence of reinfection.

HOW SUPPLIED Griseofulvin Powder (microsize) 15-gram packets (2.5 grams of griseofulvin, microsize), carton of 50; and 15-gram bottles (2.5 grams of griseofulvin, microsize) carton of 12.

Store between 2° and 30°C (36° and 86°F).

Iss1105

780504

Manufactured by
IVX Animal Health, Inc.
Fort Dodge, IA 50501

••◀ TEAR HERE ••••• TEAR HERE ▶••

NDC-0061-0960-01

Net Wt. 15 Grams

Contains

25g

Active Ingredient

Fulvicin U/F®

(GRISEOFULVIN, MICROSIZED)

POWDER

Veterinary

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

NADA #39-792, Approved by FDA.



Schering-Plough Animal Health

Schering-Plough Animal Health



16533106

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Schering-Plough Animal Health Corp., Kenilworth, NJ 07033.

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Packaged for: Schering-Plough Animal Health

Read accompanying directions carefully.

Store between 2° and 30°C (36° and 86°F).

Usual Dose: One half to one packet daily.

Indication: Equine ringworm infection caused by Trichophyton equinum or Microsporum gypsum.

For oral administration to horses—not for use in horses intended for food. The powder may be given on a small amount of feed or in a drench.

POWDER

(GRISEOFULVIN, MICROSIZED)

Fulvicin U/F®

••◀ TEAR HERE ••••• TEAR HERE ▶••

F-16521019

**PRODUCT
INFORMATION**

NADA #39-792, Approved by FDA.

FULVICIN U/F[®]
**(GRISEOFULVIN,
MICROSIZE)**

**Powder
Veterinary**

For Oral Use In Horses



CAUTION Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION FULVICIN U/F Powder is available in 15-gram packets each containing 2.5 grams griseofulvin (microsize). FULVICIN U/F is an orally effective antifungal antibiotic specifically active against superficial fungi which cause tinea (ringworm) of the skin and hair. This microsize form of griseofulvin differs from the regular FULVICIN[®] product in that its finer particle size results in a much greater surface area for absorption. An increased blood level has been obtained in experimental studies in man using fine particle size griseofulvin, indicating better absorption and a greater amount of the drug available for fungistatic action in the skin and hair.

GENERAL CONSIDERATIONS In human medicine, FULVICIN U/F (griseofulvin, microsize) is indicated in the treatment of infections caused by dermatophytic fungi of the skin, hair, and nails. Of those organisms which cause these conditions, the following are responsive to oral therapy with FULVICIN U/F: *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Trichophyton schoenleinii*, *Trichophyton sulphureum*, *Trichophyton verrucosum*, *Trichophyton interdigitale*, *Epidermophyton floccosum*, *Microsporum gypseum*, *Microsporum canis*, *Microsporum audouini*. FULVICIN U/F is inactive against bacteria and yeasts including *Monilia*, *Actinomyces*, *Nocardia*, *Blastomyces*, *Coccidioides*, *Histoplasma*, *Cryptococcus*, *Sporotrichum*, and *Aspergillus*.

The FULVICIN U/F product is administered orally until the fungi have been eliminated from the skin and hair. The length of therapy will vary with the severity of the infection. The time necessary for the newly formed, fungal-resistant keratin to reach the surface varies greatly with different structures, such as hair and thin body skin. Experimental and clinical work indicates that animals showing involvement of skin and hair only may require treatment for 3 to 4

weeks. Cure is considered complete when repeated cultures are negative for the presence of fungi. In the absence of these tests, therapy should be continued until lesions are clinically improved and there is evidence of resumed hair growth.

The infected skin in many cases shows a remarkably rapid improvement, with decreased itching and inflammation occurring in a few days. In some cases the skin may appear normal clinically in as short a time as 10 days. Viable fungi in the outer layers may persist, however, and the possibility of reinfection is not known with certainty. The optimal period of treatment has not yet been determined. Clipping of the hair to help remove any remaining viable fungi is indicated. Hair that is clipped from the infected lesion should be burned.

INDICATIONS Equine—Ringworm infection caused by *Trichophyton equinum* and *Microsporum gypseum*.

Adults—1 packet per day (2.5 grams).

Yearlings— $\frac{1}{2}$ to 1 packet per day (1.25-2.5 grams).

Foals— $\frac{1}{2}$ packet per day.

Cases of ringworm in horses caused by *T. equinum* and *M. gypseum* should be treated with the FULVICIN U/F product for a period of not less than 10 days. Responsive cases may show clinical signs of recovery in 5 to 7 days after griseofulvin therapy is initiated. In responsive cases, treatment should be continued until all infected areas are negative by appropriate culture.

If cases do not respond to therapy in 3 weeks, it is recommended that the diagnosis be reevaluated.

The powder may be given on a small amount of feed or in a drench.

Not for use in horses intended for food.

WARNING The safety and efficacy of prophylactic use of griseofulvin has not been established. This drug should not be used to treat minor or trivial infections.

Safety of griseofulvin for use in pregnant animals has not been established. It has been reported in the Soviet literature (N.N. Slonitskaya; Teratogenic Effect of Griseofulvin-Forte on the Rat Fetus/Antibiotiki 14(1):44-48, 1969) that a griseofulvin preparation was found to be embryotoxic and teratogenic on oral administration to pregnant Wistar rats. In addition, pups and kittens with either cleft palates or other abnormalities have been reported in litters of bitches and queens treated with griseofulvin during gestation.

PRECAUTIONS Patients on prolonged therapy with any potent medication should be under close observation. Periodic monitoring of organ system function, including renal, hepatic, and hemopoietic, should be done.

**PRODUCT
INFORMATION**

FULVICIN U/F[®]
**(GRISEOFULVIN,
MICROSIZE)**

**Powder
Veterinary**
For Oral Use In Horses

This antibiotic is derived from a species of *Penicillium griseofulvum*. A number of known penicillin-sensitive humans have been treated with griseofulvin without difficulty. In veterinary medicine, the drug apparently has no allergic properties; however, considerably more experience in this area must be obtained before definite conclusions may be drawn.

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In the human, heartburn, nausea, epigastric discomfort, and diarrhea have occasionally been reported. In a few instances, urticaria or drug rashes have developed and in these instances the drug should be withdrawn. Generally, the incidence of side effects has been quite low and the drug seems to be well tolerated when given orally.

The veterinarian is alerted to the following griseofulvin-associated side effects which have been reported in either human or veterinary literature: irritability, dizziness, memory loss, visual disturbances, antagonism to barbiturates and other drugs metabolized by the liver, such as warfarin-type anticoagulants.

It has also been reported that griseofulvin

affects disturbances in porphyrin metabolism, formation of hepatomata and cocarcinogenicity with methylcholanthrene; also, higher fat diet increases absorption of the antibiotic.

GENERAL MEASURES Clearing of dermatophytic infections with oral griseofulvin therapy is a great advance. However, it is necessary to maintain general hygienic precautions. The possibility of recurrence is not known. Destruction of old bedding, disinfection of stall, a close clipping of hair just before termination of therapy, etc., are measures which should reduce incidence of reinfection.

HOW SUPPLIED FULVICIN U/F Powder, 15-gram packets (2.5 grams of griseofulvin, microsize), carton of 50.

Store between 2° and 30°C (36° and 86°F).

September 1992

Schering-Plough Animal Health Corp.,
Kenilworth, New Jersey 07033

B-16521019

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50 Packets
15 g Each
10890608

2.5 g
GRISEOFULVIN
Per Packet

For oral administration to horses - not for use in horses intended for food.
Indication: Equine ringworm infection caused by *Trichophyton equinum* or *Microsporum gypseum*.
Usual Dose: One-half to one packet daily. The powder may be given on a small amount of feed or in a trench.
Store between 2° and 30° C (36° and 86° F).
Read accompanying directions carefully.

Packaged for Schering-Plough Animal Health.
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AP911140173

FULVICIN

50 MASTER

8 3/4 X 7 1/8 X 4 1/2

Must be sold in unbroken package only.

NDC-0067-0960-01

50 Packets

15 g Each

10890608

Fulvicin U/Fo Powder

(GRISEOFULVIN, MICROSIZE)

Veterinary

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

NADA 141-39-782 Approved by FDA

Schering-Plough Animal Health



2.5 g
GRISEOFULVIN
Per Packet

NDC 0061-0960-01

50 Packets

15 g Each

10890608

2.5 g
GRISEOFULVIN
Per Packet

For oral administration to horses - not for use in horses intended for food

Indication: Equine ringworm infection caused by *Trichophyton equinum* or *Microsporum gypseum*.

Usual Dose: One-half to one packet daily. The powder may be given on a small amount of feed or in a drench.

Store between 2° and 30° C (36° and 86° F)

Read accompanying directions carefully.

Packaged for Schering-Plough Animal Health

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AP911140173
FULVICIN
50 MASTER
8 3/4 X 7 1/8 X 4 1/2

Must be sold in unbroken package only

NDC 0061-0960-01
50 Packets
15 g Each
10890608

2.5 g
GRISEOFULVIN
Per Packet

Fulvicin U/F[®] Powder
(GRISEOFULVIN, MICROSIZE)

Veterinary

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NADA #39-792, Approved by FDA

Schering-Plough Animal Health

