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

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
Grieseofulvin Microsize

Veterinary Powder NET WEIGHT: 15 grams

Combines 25 active ingredients

Store between 2° and 30°C

Manufactured by RX Animal Health, Inc.

For Dose: 1A no. 5001

Veterinary

Take time

Observe label

Dose: One half to one whole daily

Microsporum Gypseum

Caused by Itophyton eum or

Indication: Equine Ringworm Infection

For oral administration to horses - not for use in

Exp. Date

Lot No.
Contains 2.5% Active Ingredient
NET WEIGHT: 15 Grams
ANADA 200-294, Approved by FDA
or on the order of a licensed veterinarian.
Caution: Federal law restricts this drug to use by
Veterinary Microsize Griseofulvin Powder
NCIC 59130-767-83

Read accompanying directions carefully.
Store between 2°C and 25°C (36°F and 77°F).
Usual dose: One tablet to one packet daily.
Instructions: Equaling Infection caused by Microsporum Gypseum.
The powder may be given in a small amount of feed or a drink.
For oral administration to horses – not for use in horses intended for food.
GRISOFULVIN 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 Grisefulvin Powder (microsize) is available in 15-gram packets and 15-gram bottles each containing 2.5 grams griseofulvin (microsize). Grisefulvin 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 Grisofulvin 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, Grisofulvin 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 Grisofulvin Powder (microsize): Trichophyton mentagrophytes, Trichophyton rubrum, Trichophyton schoenleinii, Trichophyton sulphureum, Trichophyton verrucosum, Trichophyton interdigitale, Epidermophyton floccosum, Microsporum gypseum, Microsporum canis, Microsporum audouinii. Grisofulvin Powder (microsize) is inactive against bacteria and yeasts including Monilia, Actinomycoses, Nocardia, Blastomyces, Coccidioides, Histoplasma, Cryptococcus, Sporotrichum, and Aspergillus.

The Grisofulvin 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 Microsporum gypseum.

Adults - 1 packet or bottle per day (2.5 grams).
Yearlings - 1/2 to 1 packet or bottle per day (1.25 to 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 Grisofulvin 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 allergic 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 hepatoma 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 12; 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
Fulvicin U/F
GRISEOFULVIN, MICROSIZE
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

Read accompanying directions carefully.

Store between 15° and 30°C (59° and 86°F).

Usual Dose: One half to one packet daily.

Indications: Equine ringworm infections caused by

For oral administration to horses—not for use in horses

Fulvicin U/F
GRISEOFULVIN, MICROSIZE
POWDER
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 sulphuratum, Trichophyton verrucosum, Trichophyton interdigitale, Epidermophyton floccosum, Microsporum gypseum, Microsporum canis, Microsporum audouini. FULVICIN U/F is inactive against bacteria and yeasts including Staphylococcus, 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—½ to 1 packet per day (1.25-2.5 grams).
Foals—½ 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 (I.N. Storlets-kaya, 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.
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, considerable experience in this area must be obtained before definite conclusions may be drawn.

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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), case of 50.

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

September 1992
Schering-Plough Animal Health Corp.,
Kenilworth, New Jersey 07033
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°C and 30°C (36°F and 86°F).

Read accompanying directions carefully.

Packaged for Schering-Plough Animal Health.

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

Indication: Equine ringworm infection caused by *Trichophyton equinum*.

*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°C and 30°C (36°F 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
Fulvicin U/F® Powder
(GRISOFULVIN, MICROSIZE)
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

Must be sold in unbroken package only.