The injectable solution is **compatible** with sodium chloride 0.9%, dextrose 5% in sodium chloride 0.45% or 0.9%, and dextrose 5% in water. It is compatible with many drugs at intravenous Y-sites, but is **incompatible** with amphotericin B.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Granisetron Oral Tablets: 1 mg (1.12 mg as HCl); *Kytril*® (Roche); (Rx)

Granisetron Oral Solution: 0.2 mg/mL (0.56 mg/mL as HCl, orange flavor; contains sorbitol) in 30 mL bottles; *Kytril*® (Roche); (Rx)

Granisetron Injection: 1 mg/mL (1.12 mg/mL as HCl) in 1 mL single-dose and 4 mL multi-dose vials; *Kytril*® (Roche); (Rx)

GRISEOFULVIN (MICROSIZE) GRISEOFULVIN (ULTRAMICROSIZE)

(gri-see-oh-***ful***-vin) Fulvicin®

ANTIFUNGAL AGENT

Prescriber Highlights

- Fungistatic antibiotic used primarily for ringworm & other dermatophytic infections; no effect on other fungi
- Contraindications: Pregnancy, known hypersensitivity, or hepatocellular failure
- Caution: Kittens may be overly sensitive to the drug; cats with FIV
- Adverse Effects: Anorexia, vomiting, diarrhea, anemia, neutropenia, leukopenia, thrombocytopenia, depression, ataxia, hepatotoxicity, or dermatitis/photosensitivity
- Known teratogen in cats
- Only new hair & nail growth resistant to fungi after treating
- Dosing is different for microsize & ultramicrosize forms

Uses/Indications

In veterinary species, griseofulvin is approved for use in dogs and cats to treat dermatophytic fungal (see below) infections of the skin, hair and claws, and to treat ringworm (caused by *T. equinum* and *M. gypseum*) in horses. It has also been used in laboratory animals and ruminants for the same indications. The oral tablets approved for dogs and cats are no longer marketed in the USA, but human dosage forms are available.

Pharmacology/Actions

Griseofulvin acts on susceptible fungi by disrupting the structure of the cell's mitotic spindle, arresting the metaphase of cell division. Griseofulvin has activity against species of *Trichophyton*, *Microsporum* and *Epidermophyton*. Only new hair and nail growth is resistant to infection. It has no antibacterial activity and is not clinically useful against other pathogenic fungi, including Malessezia yeasts.

Pharmacokinetics

The microsized form of the drug is absorbed variably (25–70%); dietary fat will enhance absorption. The ultramicrosize form of the drug may be nearly 100% absorbed. Generally, the ultramicrosize form is absorbed 1.5 times as well as the microsized form for a given patient.

Griseofulvin is concentrated in skin, hair, nails, fat, skeletal muscle, and the liver, and can be found in the stratum corneum within 4 hours of dosing.

Griseofulvin is metabolized by the liver via oxidative demethylation and glucuronidation to 6-desmethylgriseofulvin, which is not active. In humans, the half-life is 9–24 hours. A serum half-life of 47 minutes has been reported for dogs. Less than 1% of the drug is excreted unchanged in the urine.

Contraindications/Precautions/Warnings

Griseofulvin is contraindicated in patients hypersensitive to it or with hepatocellular failure. It should not be used in pregnant animals.

Because kittens may be overly sensitive to the adverse effects associated with griseofulvin, they should be monitored carefully if treatment is instituted. Cats should be tested for FIV before using griseofulvin because of the possible neutropenic or panleukopenic effects of the drug.

Adverse Effects

Griseofulvin can cause anorexia, vomiting, diarrhea, anemia, neutropenia, leukopenia, thrombocytopenia, depression, ataxia, hepatotoxicity, dermatitis/photosensitivity and toxic epidermal necrolysis. With the exception of GI clinical signs, adverse effects are uncommon at usual doses. Cats, particularly kittens, may be more susceptible to adverse effects (*e.g.*, bone marrow depression) than other species. This could be due to this species' propensity to more slowly form glucuronide conjugates and thus metabolize the drug at a slower rate than either dogs or humans.

Reproductive/Nursing Safety

Griseofulvin is a known teratogen in cats and, probably, in dogs as well. Dosages of 35 mg/kg given to cats during the first trimester caused cleft palate and other skeletal and brain malformations in kittens. Griseofulvin may also inhibit spermatogenesis. Because dermatophytic infections are not generally life-threatening and alternative therapies are available, use of the drug should be considered contraindicated during pregnancy. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***D*** (*Contraindicated. These drugs have been shown to cause congenital malformations or embryotoxicity.*)

No lactation safety information was found.

Overdosage/Acute Toxicity

No specifics regarding griseofulvin overdosage or acute toxicity were located. It is suggested that significant overdoses be handled with gut emptying, charcoal and cathartic administration unless contraindicated. Contact a poison control center for more information.

Horses have received 100 mg/kg PO for 20 days without apparent ill effect.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving griseofulvin and may be of significance in veterinary patients:

- **ALCOHOL:** Griseofulvin may potentiate the effects of alcohol
- **ASPIRIN:** Griseofulvin may decrease salicylate levels
- **CYCLOSPORINE:** Griseofulvin may decrease cyclosporine levels
- **PHENOBARBITAL:** Phenobarbital and other barbiturates have been implicated in causing decreased griseofulvin blood concentrations, presumably by inducing hepatic microsomal enzymes and/or reducing absorption. If phenobarbital and griseofulvin are given concurrently, griseofulvin dosage adjustment may be necessary.
- **THEOPHYLLINE:** In some patients, griseofulvin may decrease theophylline half-life and levels
- **WARFARIN:** Coumarin anticoagulants may have their anticoagulant activity reduced by griseofulvin; anticoagulant adjustment may be required

Doses

Note: all doses are for microsize preparations unless otherwise indicated.

- **DOGS:**

  For susceptible dermatophytic infections:

  a) Microsize: 25 mg/kg q12h PO for 42–56 days; Ultramicrosize: 5–10 mg/kg PO once daily for 42 days. May need to treat longer for Trichophyton than for Microsporum. Give following a fatty meal or administration of corn oil. Continue for at least 2 weeks after resolution of signs and at least 5 months for onychomycosis. (Greene, Hartmannn et al. 2006)

  b) Microsize: 50 mg/kg PO once daily with fatty meal. Used with topical therapy (see references). May double dose in resistant cases. If GI distress occurs may divide dose and give twice daily with food. Prolonged course of therapy required. Begin taking cultures after 4 weeks of treatment. Continue therapy for 2 weeks beyond clinical cure and when 2–3 negative cultures are obtained at weekly intervals. (Frank 2000)

- **CATS:**

  For susceptible dermatophytic infections:

  a) Microsize: 50–120 mg/kg PO; divided daily. Give with a fatty meal. Ultramicrosize: 10–15 mg/kg PO twice daily. Give for 4–6 weeks or longer, until culture is negative. (Foil 2003b)

  b) Microsize: 50 mg/kg PO once daily or 25 mg/kg PO q12h for 42–70 days; Ultramicrosize: 5–10 mg/kg PO once daily for 42 days. Give following a fatty meal or administration of corn oil. Continue for at least 2 weeks after resolution of signs and at least 5 months for onychomycosis. (Greene, Hartmannn et al. 2006)

  c) For feline *M. canis*: After total body clip, griseofulvin 80–130 mg/kg PO once daily with a fatty meal or 2.5–5 mL of corn oil. Re-clip after one month and continue treatment until signs of infection have disappeared and cultures are negative. (Thoday 1986)

  d) Microsize: 50 mg/kg PO once daily with fatty meal. Used with topical therapy (see references). May double dose in resistant cases. If GI distress occurs may divide dose and give twice daily with food. Prolonged course of therapy required. Begin taking cultures after 4 weeks of treatment. Continue therapy for 2 weeks beyond clinical cure and when 2–3 negative cultures are obtained at weekly intervals. (Frank 2000)

  e) For feline eosinophilic granuloma complex: Microsize: 25 mg/kg PO twice daily with food. Give at least for one month to judge efficacy. (White 2003b)

- **RABBITS/RODENTS/SMALL MAMMALS:**

  a) Rabbits for advanced dermatophytosis: Ultramicrosize 6.25 mg/kg PO q12h for 4–6 weeks. Microsize: 25 mg/kg PO q12–24h for one month (Ivey and Morrisey 2000)

  b) Chinchillas: 25 mg/kg PO once daily for 30–60 days (Hayes 2000)

  c) Gerbils, Guinea pigs, Hamsters, Rats: 25 mg/kg PO q24h for 14–28 days; Mice: 25 mg/kg PO q24h for 14 days; Chinchillas: 25 mg/kg PO q24h for 28–40 days (Adamcak and Otten 2000)

  d) Guinea pigs for dermatophytosis: 25 mg/kg PO (as a suspension) once daily for 28 days. (Johnson 2006d)

  e) Chinchillas: 25 mg/kg PO once daily (q24h) for 30 days (Johnson 2006a)

- **CATTLE** (and other ruminants):

  For susceptible dermatophytic infections:

  a) Ultramicrosize: 10–20 mg/kg PO once daily for 1–2 weeks. 100 mg/kg PO given twice (or more) 1 week apart may also be effective. Not approved for use in food animals and can be very expensive. (Pier 1986)

  b) 20 mg/kg PO once daily for 6 weeks (Howard 1986)

- **HORSES:**

  For susceptible dermatophytic infections:

  a) 10 mg/kg PO once daily (Robinson 1987)

  b) 10 mg/kg PO (in feed) daily for 7 days (Brumbaugh 1987)

- **SWINE:**

  For susceptible dermatophytic infections:

  a) 20 mg/kg PO once daily for 6 weeks (Howard 1986)

- **BIRDS:**

  a) Ratites: 35–50 mg/kg PO once daily (Jenson 1998)

Monitoring

- Clinical efficacy; culture
- Adverse effects
- CBC; before therapy and q1–3 weeks during therapy
- Liver enzymes (if indicated)

Client Information

- Clients should be instructed in procedures used to prevent reinfection (destruction of old bedding, disinfection, periodic reexaminations, hair clipping, etc.), and the importance of compliance with the dosage regimen.
- Should animal develop adverse effects other than mild GI disturbances, they should contact their veterinarian.

Chemistry/Synonyms

A fungistatic antibiotic produced by species of Penicillium (primarily *P. griseofulvum*), griseofulvin occurs as an odorless or nearly odorless, bitter tasting, white to creamy white powder. It is very slightly soluble in water and sparingly soluble in alcohol.

Two forms of the drug are available commercially. Microsize griseofulvin contains particles with a predominant size of 4 micrometers in diameter, while the ultramicrosize form particle size averages less than 1 micron in diameter.

Griseofulvin may also be known as: curling factor, griseofulvina, and griseofulvinum; many trade names are available.

Storage/Stability/Compatibility

Although griseofulvin is relatively thermostable, products should be stored at less than 40°C, preferably at 15–30°C. Griseofulvin suspension should be stored in tight, light-resistant containers. Microsize tablets and capsules should be stored in tight containers; the ultramicrosize tablets should be stored in well-closed containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Griseofulvin (Microsize) Powder: 2.5 g griseofulvin in 15 g sachets; *AmTech® Griseofulvin Powder* (IVX); (Rx). Approved for use in horses not intended for food.

HUMAN-LABELED PRODUCTS:

Griseofulvin Microsize Tablets: 500 mg; *Grifulvin V®* (Ortho); (Rx)

Griseofulvin Microsize Oral Suspension: 125 mL/5 mL in 120 mL; *Grifulvin V®* (Ortho); generic; (Rx)

Griseofulvin Ultramicrosize Tablets: 125 mg & 250 mg; *Gris-PEG®* (Pedinol); (Rx)

GUAIFENESIN

(gwye-***fen***-e-sin) GG, Guailaxin®

PARENTERAL MUSCLE RELAXANT/ORAL EXPECTORANT

Prescriber Highlights

- An expectorant (oral) & muscle relaxant (parenteral) adjunctive to anesthesia
- Contraindications: None noted except concurrent use with physostigmine
- Adverse Effects: Mild hypotensive effect & increase in cardiac rate, thrombophlebitis possible

Uses/Indications

In veterinary medicine, guaifenesin is used to induce muscle relaxation and restraint as an adjunct to anesthesia for short procedures (30–60 minutes) in large and small animal species. There are combination oral products containing guaifenesin for treating respiratory conditions in horses.

In human medicine, guaifenesin has long been touted as an oral expectorant, but definitive proof of its efficacy is lacking.

Pharmacology/Actions

While the exact mechanism of action for the muscle relaxant effect is not known, it is believed that guaifenesin acts centrally by depressing or blocking nerve impulse transmission at the internuncial neuron level of the subcortical areas of the brain, brainstem and spinal cord. It relaxes both the laryngeal and pharyngeal muscles, thus allowing easier intubation. Guaifenesin also has mild intrinsic analgesic and sedative qualities.

Guaifenesin causes an excitement-free induction and recovery from anesthesia in horses. It produces relaxation of skeletal muscles but does not affect diaphragmatic function and has little, if any, effect on respiratory function at usual doses. Possible effects on the cardiovascular system include transient mild decreases in blood pressure and increases in cardiac rate. Gastrointestinal motility may be increased, but generally no adversity is seen with this.

Guaifenesin potentiates the activity of preanesthetic and anesthetic agents.

Pharmacokinetics

The pharmacokinetics of guaifenesin have not been thoroughly studied in most species. When administered alone to horses IV, recumbency usually occurs within 2 minutes and light (not surgical level) restraint persists for about 6 minutes. Muscle relaxation reportedly persists for 10–20 minutes after a single dose.

Guaifenesin is conjugated in the liver and excreted into the urine. A gender difference in the elimination half-life of guaifenesin in ponies has been demonstrated, with males having a $t_{1/2}$ of approximately 85 minutes, and females a $t_{1/2}$ of about 60 minutes. Guaifenesin reportedly crosses the placenta, but adverse effects in newborns of mothers who received guaifenesin have not been described.

Contraindications/Precautions/Warnings

The manufacturer states that the use of physostigmine is contraindicated with guaifenesin (see Drug Interactions).

Adverse Effects

At usual doses, side effects are transient and generally minor. A mild decrease in blood pressure and increase in cardiac rate can be seen. Thrombophlebitis has been reported after IV injection, and perivascular administration may cause some tissue reaction. Hemolysis may occur in solutions containing greater than a 5% concentration of guaifenesin, but some sources state this is insignificant at even a 15% concentration.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy *(Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.)*

It is not known whether guaifenesin is excreted in milk.

Overdosage/Acute Toxicity

The margin of safety is reportedly 3 times the usual dose. Clinical signs of apneustic breathing, nystagmus, hypotension, and contradictory muscle rigidity are associated with toxic levels of the drug.

There were 69 exposures to guaifenesin reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2000–2006. In these cases 59 were dogs with only 1 showing clinical signs and 8 cases were cats with only 1 showing clinical signs. The remaining 2 cases were birds which showed no clinical signs. The dog received a dosage estimated between 415 and 830 mg/kg and exhibited hypothermia, mild tremors, ataxia and vomiting. The cat received a dosage of 132 mg/kg and exhibited lethargy and anorexia.

No specific antidote is available. It is suggested that treatment be supportive until the drug is cleared to sub-toxic levels.

Drug Interactions

Drug interactions with guaifenesin are not well studied. The following drug interactions have either been reported or are theoretical in animals receiving guaifenesin and may be of significance in veterinary patients:

- **PHYSOSTIGMINE**: The manufacturer (Robins) states that physostigmine is contraindicated in horses receiving guaifenesin, but does not elucidate on the actual interaction. It may be logical to assume that other anticholinesterase agents (**neostigmine**, **pyridostigmine**, **edrophonium**) may also be contraindicated.