NYSTATIN (ORAL)

(nye-*stat*-in) Nilstat®, Mycostatin®

ANTIFUNGAL (CANDIDA)

Prescriber Highlights

- Oral & topical antifungal (Candida); not absorbed systemically after PO
- Contraindications: Known hypersensitivity
- Adverse Effects: GI effects possible at high dosages; hypersensitivity possible

Uses/Indications

Orally administered nystatin is used primarily for the treatment of oral or gastrointestinal tract Candida infections in dogs, cats, and birds; it has been used less commonly in other species for the same indications.

Pharmacology/Actions

Nystatin has a mechanism of action similar to that of amphotericin B. It binds to sterols in the membrane of the fungal cell altering the permeability of the membrane allowing intracellular potassium and other cellular constituents to "leak out."

Nystatin has activity against a variety of fungal organisms, but is clinically used against topical, oropharyngeal, and gastrointestinal Candida infections.

Pharmacokinetics

Nystatin is not measurably absorbed after oral administration and almost entirely excreted unchanged in the feces. The drug is not used parenterally because it is reportedly extremely toxic to internal tissues.

Contraindications/Precautions/Warnings

Nystatin is contraindicated in patients with known hypersensitivity to it.

Adverse Effects

Occasionally, high dosages of nystatin may cause GI upset (anorexia, vomiting, diarrhea). Rarely, hypersensitivity reactions have been reported in humans.

Reproductive/Nursing Safety

Although the safety of the drug during pregnancy has not been firmly established, the lack of appreciable absorption or case reports associating the drug with teratogenic effects appear to make it safe to use. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

It is not known whether nystatin is excreted in maternal milk, but because the drug is not absorbed after oral administration it is unlikely to be of concern.

Overdosage/Acute Toxicity

Because the drug is not absorbed after oral administration, acute toxicity after an oral overdose is extremely unlikely, but transient GI distress may result.

Drug Interactions

No significant interactions reported for oral nystatin

Doses

DOGS:

For oral treatment of Candidal infections:

a) 100,000 Units PO q6h (Kirk 1989)

b) 50,000–150,000 Units PO q8h (Jenkins and Boothe 1987)

c) 22,000 Units/kg/day (Huber 1988b)

CATS:

For oral treatment of Candidal infections:

a) 100,000 Units PO q6h (Kirk 1989)

HORSES:

For intrauterine infusion:

a) 250,000–1,000,000 IU; Mix with sterile water; precipitates in saline. Little science is available for recommending doses, volume infused, frequency, diluents, etc. Most intrauterine treatments are commonly performed every day or every other day for 3–7 days. (Perkins 1999)

BIRDS:

For crop mycosis and mycotic diarrhea (*Candida albicans*) in chickens and turkeys:

a) Feed at 50 grams per ton (*Mycostatin®-20*) or at 100 g/ton for 7–10 days. (Label directions; *Mycostatin®-20*—Solvay)

For enteric yeast (Candidal) infections:

a) 200,000–300,000 units/kg PO q8–12h. Relatively large volume must be administered (2–3 mL). May also be used prophylactically to prevent yeast infection in nestling birds treated with broad-spectrum antibiotics. Oral lesions may be missed if bird is tubed. (Flammer 2003a)

b) For neonates on antibiotic therapy: Crush one fluconazole 100 mg tablet and mix with 20 mL of nystatin 100,000U/mL oral suspension. Dose at 0.5 mL/1000g of body weight PO twice daily for duration of antibiotic therapy. (Wissman 2003)

c) For treatment of candidiasis after antibiotic or in conjunction with antibiotics: One mL of the 100,000 U/mL suspension per 300 g body weight PO 1–3 times daily for 7–14 days. If treating mouth lesions do not give by gavage. Hand-fed babies should receive antifungal therapy if being treated with antibiotics. (Clubb 1986)

Ratites:

a) 250,000–500,000 IU/kg PO twice daily (Jenson 1998)

REPTILES:

For susceptible infections:

a) For turtles with enteric yeast infections: 100,000 IU/kg PO once daily for 10 days (Gauvin 1993)

b) All species: 100,000 units/kg PO once daily (Jacobson s1999)

Monitoring

- Clinical efficacy

Client Information

- Shake suspension well before administering

Chemistry/Synonyms

A polyene antifungal antibiotic produced by *Streptomyces noursei*, nystatin occurs as a yellow to light tan, hygroscopic powder having a cereal-like odor. It is very slightly soluble in water and slightly to sparingly soluble in alcohol. One mg of nystatin contains not less than 4400 Units of activity. According to the USP, nystatin used in

the preparation of oral suspensions should not contain less than 5000 Units per mg.

Nystatin may also be known as: fungicidin, nistatina, or nystatinum, *Mycostatin*®, and *Nilstat*®.

Storage/Stability

Nystatin tablets and oral suspension should be stored at room temperature (15–30°C) in tight, light-resistant containers. Avoid freezing the oral suspension or exposing to temperatures greater than 40°C.

Nystatin deteriorates when exposed to heat, light, air or moisture.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

None, for oral use. For topical use, see the topical dermatologic section in the appendix.

HUMAN-LABELED PRODUCTS:

Nystatin Oral Suspension: 100,000 Units/mL in 5 mL, 60 mL, 473 mL and 480 mL; *Nilstat*® (Lederle); generic; (Rx)

Nystatin Bulk powder: 50 million, 150 million, 500 million units, 1 billion, 2 billion and 5 billion units; generic; (Paddock); *Nilstat*® (Lederle); (Rx)

Nystatin Oral Tablets: 500,000 Units; *Mycostatin*® (Bristol-Myers Squibb), generic; (Rx)

Also available in oral troches, vaginal tablets, topical creams, powders and ointments.

OCTREOTIDE ACETATE

(ok-*trye*-oh-tide) Sandostatin®

SOMATOSTATIN ANALOG

Prescriber Highlights

- Injectable long acting somatostatin analog that may be useful for adjunctive treatment of insulinomas & gastrinomas
- Limited experience, but appears safe
- Multiple daily SC injections are required
- No information for veterinary use of depot IM form
- Expensive (especially in large dogs)
- May affect GI fat absorption

Uses/Indications

Octreotide may be useful in the adjunctive treatment of hyperinsulinemia in patients with insulinomas (especially dogs, ferrets). Response is variable, presumably dependent on whether the tumor cells have receptors for somatostatin. Octreotide may also be useful in the diagnosis and symptomatic treatment of gastrinomas in dogs or cats. It may be of use in the treatment of acute pancreatitis, but more research is needed before it can be recommended for this use in veterinary patients.

Pharmacology/Actions

Octreotide is a synthetic long acting analog of somatostatin. It inhibits the secretion of insulin (in both normal and neoplastic beta cells), glucagon, secretin, gastrin and motilin. In humans, octreotide may bind to any one of 5 subtypes of somatostatin receptors found on neoplastic beta cells, but dogs only have one subtype. This, or octreotide's inhibition of glucagon and growth hormone secretion, may explain the variable response dogs have to treatment.

Pharmacokinetics

Octreotide is absorbed and distributed rapidly from the injection site after SC administration. Half lives in humans average about 2 hours with duration of effect up to 12 hours. Treated dogs or ferrets generally require 2–3 injections per day to maintain blood glucose. About 32% of a dose is excreted unchanged in the urine and patients with severe renal dysfunction may need dosage adjustment.

Contraindications/Precautions/Warnings

Octreotide is contraindicated in patients hypersensitive to it. It should be used with caution in patients with biliary tract disorders.

Adverse Effects

Very limited experience in domestic animals, although it appears to be well tolerated thus far. GI effects (including biliary tract effects) are most commonly noted in human patients, particularly acromegalics.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

It is not known whether this drug is excreted in maternal milk.

Overdosage/Acute Toxicity

Serious adverse effects are unlikely. Human subjects have received up to 120 mg IV over 8 hours with no untoward effects.

Drug Interactions

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

- **BETA-BLOCKERS:** Octreotide may cause additive bradycardic effects
- **BROMOCRIPTINE:** Octreotide may increase oral bioavailability
- **CALCIUM-CHANNEL BLOCKERS:** Octreotide may cause additive bradycardic effects
- **CYCLOSPORINE:** Octreotide may reduce cyclosporine levels
- **DIURETICS (and other agents that affect fluid/electrolyte balance):** Octreotide may enhance fluid/electrolyte imbalances
- **FOOD:** Octreotide may reduce fat absorption
- **INSULIN, ORAL HYPOGLYCEMICS:** Octreotide may can inhibit insulin
- **QUINIDINE:** Octreotide may reduce the quinidine clearance

Doses

- Dogs:

  For medical treatment of insulinoma (particularly in patients refractory to or unable to tolerate other medical or surgical therapy):

  a) 10–40 mcg (total dose per dog) SC 2–3 times a day. Used in combination with dietary, glucocorticoid, and diazoxide treatment. (Nelson 2000)

  b) Further studies needed to determine octreotide's efficacy and safety; has been administered at 2–4 mcg/kg SC q8–12h (Hess 2005)