

Ketoconazole

- Drug Information

Brand Names:

Nizoral®

Pharmacology:

Imidazole antifungal agent

Indications:

Used as an antifungal agent in the treatment of many mycoses in small animals.
Also used as an alternative treatment for hyperadrenocorticism.

Contraindications:

- General

Contraindicated in patients with known sensitivity to this type of drug.
Use with caution in patients with liver disease or thrombocytopenia.
Contraindicated in pregnancy as stillbirth may result.

Interactions:

- General Interactions

Use with extreme caution with other drugs that have hepatotoxic potential.

- Category Interactions

- Antacid

Antacids may inhibit absorption. Separate doses by 2 hours.

- Anticholinergic

Anticholinergics may inhibit absorption. Separate doses by 2 hours.

- H-2 Antagonist

H2 blockers may inhibit absorption. Separate doses by 2 hours.

- Hepatic enzyme inhibitor

Metabolism of other cytochrome P-450 metabolized drugs may be altered.

- Protein bound drug

May displace other highly protein bound drugs resulting in increased activity of both.

- Drug Interactions

- Acyclovir

Synergistic with acyclovir against herpes simplex virus.

- Aminophylline

May decrease theophylline serum levels.

- Cisapride

May inhibit the metabolism of cisapride and result in high plasma concentrations of cisapride which has been associated with fatal cardiac arrhythmias in humans.

- ClomiPRAMINE

Metabolism of ClomiPRAMINE may be inhibited by ketoconazole.

- CycloSPORINE

May increase CycloSPORINE serum levels.

- Itraconazole

Metabolism of ClomiPRAMINE may be inhibited by itraconazole.

- MethylPREDNISolone

MethylPREDNISolone activity may be prolonged.

- Mitotane

Mitotane is contraindicated as adrenolytic effects may be inhibited.

- Omeprazole

Omeprazole may increase gastric acid pH, resulting in decreased absorption of ketoconazole.

- PHENobarbital

PHENobarbital speeds the metabolism of ketoconazole.

- Phenytoin sodium

Phenytoin may affect metabolism of ketoconazole and increase the risk of toxicity of each.

- Rifampin

Rifampin may decrease serum levels of ketoconazole..

- Theophylline

May decrease theophylline serum levels.

- Warfarin sodium

May increase the anticoagulant effects of warfarin.

Adverse Effects:

- General

Vomiting, diarrhea, loss of appetite, weight loss, photophobia, gingival bleeding, paraesthesia are possible side effects of this medication.

Hepatic toxicity-cholangiohepatitis, increased hepatic enzymes.

Thrombocytopenia is a rare reaction.

Pruritus, alopecia and reversible lightening of hair coat are also possible.

- Small Animal

- Dog

Male dog reversible infertility has been reported that responds to withdrawal of the drug.

Cataract formation may result with long term use.

Suppresses serum cortisol levels in dogs with hyperadrenocorticism-dogs on high dose may need additional glucocorticoids during stress.

- Cat

Cats are more prone to hepatotoxic and GI effects.

Dosages:

- General

For specific information regarding protocols, see specialized reference material.

Give with food.

- Small Animal

- Dog

Coccidiomycosis- 5 - 20 mg/kg by mouth twice daily for 6 - 12 months. Animals with bony lesions or relapses after discontinuing therapy, give lifelong therapy at 5 mg/kg by mouth every other day.

Blastomycosis- 10 - 20 mg/kg by mouth twice daily for at least 3 months usually with amphotericin B initially at 0.25 - 0.5 mg/kg every other day IV. If tolerated, increase dose to 1 mg/kg until 4 - 5 mg/kg total dose is administered. (See amphotericin B for details)

Histoplasmosis- 5 - 10 mg/kg by mouth twice daily for 2 - 3 months.

Aspergillosis- 20 mg/kg by mouth for at least 6 weeks.

Cryptococcosis: Amphotericin B 0.15 - 0.4 mg/kg IV 3 times a week with flucytosine 150 - 175 mg/kg by mouth divided three times daily - four times daily. When a total dose of amphotericin B reaches 4 - 6 mg/kg start maintenance dosage of amphotericin B at 0.15 - 0.25 mg/kg IV once a month with flucytosine at dosage above or with ketoconazole at 10 mg/kg by mouth once daily or divided twice daily.

Fungal myocarditis- 10 mg/kg by mouth three times daily

Candidal stomatitis- 10 mg/kg by mouth three times daily

Malassezia dermatitis- 5 - 10 mg/kg by mouth twice daily for 30 days. Often used with therapeutic shampoos containing selenium disulfide, miconazole, ketoconazole or chlorhexidine.

Dermatophytosis: Usually reserved for when griseofulvin ineffective or not tolerated. 10 mg/kg by mouth once daily with an acidic meal. 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

For treatment of hyperadrenocorticism: 5 mg/kg by mouth twice a day for 7 days. If no problems with appetite or icterus, increase dose to 10 mg/kg by mouth twice a day. Repeat ACTH response test in 14 days (animal stays on drug). If not satisfactorily controlled, increase to 15 mg/kg twice a day. Goal is pre- and post-ACTH plasma cortisol levels of less than 5 microgram/kg.

- Cat

Coccidiomycosis- 5 - 20 mg/kg by mouth twice daily for 6 - 12 months.

Blastomycosis- 10 mg/kg by mouth twice daily (15 - 20 mg/kg by mouth twice daily if CNS involvement) for at least 3 months with amphotericin B: initially at 0.25 - 0.5 mg/kg every other day

IV. If tolerated, increase dose to 1 mg/kg until 4 - 5 mg/kg total dose is administered. See amphotericin B for more information.

Histoplasmosis- 10 mg/kg by mouth every 12 hours with amphotericin B at 0.25 mg/kg in 30 mL D5W IV over 15 minutes every 48 hours. Continue amphotericin B therapy for 4 - 8 weeks or until BUN > 50 mg/dL. If BUN increases greater than 50 mg/dL, continue ketoconazole alone.

Ketoconazole is used long-term (at least 6 months of duration). Despite aggressive therapy prognosis is poor.

Cryptococcosis- 10 mg/kg by mouth twice daily for at least 3 months or 30 days after clinical resolution.

Aspergillosis- 20 mg/kg by mouth for at least 6 weeks

For dermatophytosis: Usually reserved for when griseofulvin ineffective or not tolerated. 10 mg/kg by mouth once daily with an acidic meal. 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.

- Birds (small)

For susceptible fungal infections: For severe refractory candidiasis in psittacines: 5 - 10 mg/kg as a gavage twice daily for 14 days. For local effect in crop dissolve 1/4 tablet (50 mg) in 0.2 mL of 1 N hydrochloric acid and add 0.8 mL of water. Solution turns pale pink when dissolved. Add mixture to food for gavage.

To add to water for most species: 200 mg/L for 7 - 14 days. As drug is not water soluble at neutral pH, dissolve in acid prior to adding to water (see above).

To add to feed for most species: 10 - 20 mg/kg for 7 - 14 days. Add to favorite food or add to mash. For Candida infections of the oropharyngeal area: 10 - 15 mg/kg by mouth twice daily for 10 - 14 days; ratites: 5 - 10 mg/kg by mouth once daily

- Rodent

Gerbils, Mice, Rats: For systemic mycoses/candidiasis: 10 - 40 mg/kg per day by mouth for 14 days

- Rabbit

Rabbits: 10 - 40 mg/kg per day by mouth for 14 days

- Reptiles

15 - 30 mg/kg by mouth once daily for 2 - 4 weeks.

- Guinea Pig

For systemic mycoses/candidiasis: 10 - 40 mg/kg per day by mouth for 14 days

- Ferret

10 - 50 mg/kg divided by mouth three times daily

- Hamster

For systemic mycoses/candidiasis: 10 - 40 mg/kg per day by mouth for 14 days

- Turtle

For fungal shell diseases in turtles/tortoises: 25 mg/kg by mouth once a day for 2 - 4 weeks

- **Large Animal**

- Horse

10 mg/kg by mouth once daily

Special Notes:

The use of this drug in veterinary patients is considered extra-label as no veterinary approved product is available. Information regarding its use is derived from general veterinary references such as those listed in the VPR Help File under references. For additional information consult the drug manufacturer. It remains the responsibility of the prescribing veterinarian to familiarize themselves with the package insert or additional information provided by the drug manufacturer.