Ronidazole

- (roe-nid-ah-azole)
- Antiprotozoal

**Prescriber Highlights**

- Nitroimidazole antibiotic/antiparasitic drug that appears to be useful in treating *Tritrichomonas foetus* infections in cats; also used for treating trichomonas infections in non-food birds. Potentially useful as an alternative treatment for Giardia.
- Potentially carcinogenic; avoid human exposure.
- Neurotoxicity (reversible): more likely at higher doses (50 mg/kg twice daily), but can occur at lower dosages as well; GI effects possible.
- Many potential drug interactions.
- Must be compounded from bulk powder (100%) & ideally, put in gelatin capsules.

**Uses/Indications**

Ronidazole is a nitroimidazole antibiotic/antiparasitic drug that, at present, is considered the treatment of choice for *Tritrichomonas foetus* infections in cats. However a retrospective study concluded: “In most cats, ronidazole treatment at the currently recommended dosage (30 mg/kg PO q24h for 2 weeks) was efficacious in ameliorating clinical signs. However, in some cats clinical signs persisted despite use of ronidazole at the currently recommended dosages.” (Xenoulis et al. 2013)

Ronidazole may also prove to be a viable alternative treatment for giardiasis in dogs and cats. The drug is also used for treating *Trichomonas* infections in non-food animal birds.

The drug is not commercially available in the USA and must be compounded from bulk powder by a compounding pharmacy.

**Pharmacology/Actions**

Ronidazole, like other 5-nitroimidazoles such as metronidazole is converted by hydrogenosomes (an organelle found in trichomonads) into polar autotoxic anion radicals. *T. foetus* infections in cats have been resistant to treatment by metronidazole and ronidazole appears to have greater activity against the organism, but ronidazole resistance has been documented (Gookin et al. 2010).

**Pharmacokinetics**

In cats, ronidazole is completely absorbed and bioavailable after oral dosing. Volume of distribution (steady state) is ≈ 0.7 L/kg and clearance ≈ 0.8 mL/kg/min. Elimination half-life is long at ≈ 10 hours (LeVine et al. 2008).

A guar gum-coated colon-targeted delayed-release tablet formulation had negligible release until 6 hours after administration. Peak plasma levels occurred at ≈ 14.5 hours, coinciding with colonic arrival. Repeated dosing did not appreciably affect bioavailability or other pharmacokinetic parameters (Papich et al. 2013).
**CONTRAINICATIONS/RECAUTIONS/WARNINGS**

Ronidazole should not be used in patients hypersensitive to it or other 5-nitroimidazoles (e.g., metronidazole).

The compound has been demonstrated to be carcinogenic in mice but not rats. While humans should avoid contact with this compound or animal waste from treated patients, it can be safely compounded using a biological safety cabinet.

The FDA prohibits this drug for use in food animals.

**ADVERSE EFFECTS**

Reversible neurotoxicity similar to that reported with metronidazole, has been reported in cats with ronidazole. Initial signs may include tremors, lethargy, anorexia, ataxia, nystagmus, seizures or behavior changes (agitation). Should neurotoxicity be diagnosed, discontinue ronidazole, treat supportively, and if necessary, consider administering a benzodiazepine such as diazepam to competitively inhibit GABA receptors in the CNS. Incidence of neurotoxicity appears to be higher when using the 50 mg/kg twice-daily dosage, but may occur at lower dosages as well. Potentially, gastrointestinal effects can occur (anorexia, vomiting). Ronidazole is very bitter and should be administered to cats in capsule form.

Ronidazole has been shown to increase the rate of benign mammary tumors in rats and benign and malignant pulmonary tumors in mice at dosages ≥ 20 mg/kg/day.

Dogs given 30 mg/kg per day for 2 years (40 mg/kg/day the first month) showed some testicular toxicity (type not specified), but no tumors.

**REPRODUCTIVE/NURSING SAFETY**

Safety of this compound during pregnancy is not established. Teratology studies have been performed in mice, rats, and rabbits. In rabbits given 30 mg/kg/day, no embryotoxicity occurred, but fetal weights were significantly decreased. Mice demonstrated no teratogenic effects at dosages of up to 200 mg/kg/day. Rats given up to 150 mg/kg/day demonstrated no embryotoxic effects, but at dosages of 200 mg/kg/day both maternal and fetal weights were decreased.

If this compound is to be used in pregnant cats, weigh the potential benefits of treating with the potential for adverse effects in the offspring and queen.

It is not known if ronidazole is distributed into milk and safety cannot be assured. Consider using milk replacer if treating nursing queens.

**OVERDOSE/ACUTE TOXICITY**

No specific information was located. Cats receiving doses of 50 mg/kg twice daily appear to have greater incidences of neurotoxicity (see Adverse Reactions). A case report of an overdose causing neurotoxicity, hemorrhage and death in society finches after consuming ronidazole in drinking water has been published (Woods et al. 2010). If overdoses cause neurotoxicity, discontinue further therapy and treat supportively. Consider administering a GABA inhibitor such as diazepam to competitively inhibit GABA receptors in the CNS.

**DRUG INTERACTIONS**

In humans, the following drug interactions with metronidazole, a compound similar to ronidazole, have been reported or are theoretical and may be of significance in veterinary patients in patients receiving ronidazole. Unless otherwise noted, use together is not necessarily contraindicated, but weigh the potential risks and perform additional monitoring when appropriate.
Alcohol: May induce a disulfiram-like (nausea, vomiting, cramps, etc.) reaction.

Cimetidine, Ketoconazole: May decrease the metabolism of ronidazole and increase the likelihood of dose-related side effects occurring.

Cyclosporine, Tacrolimus (systemic): Ronidazole may increase the serum levels of cyclosporine or tacrolimus.

Fluorouracil (systemic): Ronidazole may increase the serum levels of fluorouracil and risk for toxicity.

Lithium: Ronidazole may increase lithium serum levels and risk for lithium toxicity.

Oxytetracycline: Reportedly may antagonize the therapeutic effects of metronidazole (and presumably ronidazole).

Phenobarbital, Rifampin or Phenytoin: May increase the metabolism of ronidazole thereby decreasing blood levels.

Warfarin: Metronidazole (and potentially ronidazole) may prolong INR/PT in patients taking coumarin anticoagulants; avoid concurrent use if possible; otherwise intensify monitoring.

LABORATORY CONSIDERATIONS

AST, ALT, LDH (lactic dehydrogenase), Triglycerides, Hexokinase glucose: A related compound, metronidazole can cause falsely decreased readings when determined using methods measuring decreases in ultraviolet absorbance when NADH is reduced to NAD. It is not known if ronidazole can also cause falsely decreased values.

DOSES

Dogs:

For Giardia (extra-label): Study was in a kennel setting and combined strict hygiene control/disinfection, chlorhexidine shampoos and ronidazole at 30 – 50 mg PO twice daily for 7 days. Authors concluded this “was highly effective in reducing Giardia cyst excretion and may therefore constitute an alternative control strategy for canine giardiasis.” (Fiechter et al. 2012)

Cats:

For treatment of *T. foetus* infections (extra-label): Recent studies investigating the pharmacokinetics of ronidazole in cats suggest that 30 mg/kg PO q24h for 14 days is likely to be most effective in resolving diarrhea and eradicating *T. foetus* infection. (Tolbert et al. 2009)

MONITORING

Clinical efficacy (diarrhea improvement).

Adverse effects (neurotoxicity, vomiting, anorexia).

PCR testing (can be used to confirm infection, but negative results after treatment do not conclusively prove that infection has been eradicated).

CLIENT INFORMATION

Keep stored in the freezer.

Give with food to avoid stomach or intestinal problems.

Side effects in cats can include fever, loss of appetite, ataxia (*e.g.*, trouble keeping balance, trouble walking or climbing stairs, etc.), muscle twitching or weakness, seizures, lethargy (tiredness/lack of energy), nystagmus (eyes uncontrollably moving back and forth). Contact veterinarian immediately if any of these signs are seen.
Has caused cancer at high doses in laboratory animals. Do not open or crush capsules; administer whole. Wear disposable gloves when handling and wash hands afterwards.

Wear disposable gloves when cleaning the litter box, double bag feces and throw both gloves and feces in trash. Do not flush feces down toilet.

Must not be used in any animals that will be consumed by humans.

**CHEMISTRY/SYNONYMS**

Ronidazole is a 5-nitroimidazole compound that occurs as a white to yellowish-brown, odorless or almost odorless, bitter-tasting, powder. It is very slightly soluble in water or alcohol.

Ronidazole may also be known as ronidazol, ronidazolum, Belga®, Ridsol-S®, Ronida®, Ronivet®, Ronizol®, Turbosol®, Tricho Plus®, Trichocure®, or Trichorex®.

**STORAGE/StABILITY**

Compounded capsules should be stored in child-resistant, tight containers protected from light. Until further stability studies can be performed, capsules should be stored in the freezer.

Aqueous solutions are reportedly not very stable. It is recommended that fresh solutions using the 10% powder for addition to drinking water (used for pigeons) be freshly prepared every day.

**COMPATIBILITY/COMPOUNDING CONSIDERATIONS**

No specific information noted. See additional information in Dosage Form section.

**DOSEAGE FORMS/REGULATORY STATUS**

**Veterinary-Labeled Products:**

None in the USA; a 10% ronidazole powder to be added to drinking water for treating Trichomonas infections in pigeons is available in some countries, but these products are unsuitable for use in cats due to the dosage required and the unpalatability (very bitter) of the powder and solution. Capsules prepared from 100% bulk powder for an individual feline patient should be obtained from a compounding pharmacy that can prepare the capsules in a bio-safety hood that will protect the compounder from drug exposure.

The FDA prohibits this drug for use in food animals.

**Human-Labeled Products:** None.

**REVISIONS/REFERENCES**

Monograph revised/updated August 2014.


