



Metronidazole Risks

Metronidazole typically has a wide margin of safety in small animals; on occasion, however, toxicity can be an issue, along with other infrequent adverse events.

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Adverse Events

- ⚠️ Although a rare occurrence, animals may be hypersensitive to metronidazole; therefore, its use should be avoided in patients with sensitivity to any nitroimidazole derivative.^{1,2}
- ⚠️ Adverse events are uncommon but have been reported, including
 - CNS signs/neurotoxicity (eg, ataxia, peripheral neuropathy, hypermetric gait, nystagmus, head tilt, seizures)¹⁻³
 - Neutropenia^{1,2}
 - GI signs (eg, vomiting, stomatitis, glossitis, diarrhea^{1,2}; anorexia, hypersalivation likely due to bitter and/or sharp metallic taste²)
 - Hepatotoxicity^{1,2}
 - Pigmenturia^{1,2}
- ⚠️ Because glucuronidation is deficient in cats, they may be more sensitive to metronidazole; high doses should thus be avoided.

Toxicities

- ⚠️ Metronidazole toxicity can occur in dogs and cats but typically involves chronic versus acute exposure.
 - Chronic doses >62 mg/kg q24h have been associated with toxicity.^{1,2}
 - Severe permanent neurologic signs may be seen with large, acute doses (>250 mg/kg).^{1,2}

Clinical Signs

- ⚠️ Signs of toxicity typically include
 - Ataxia¹⁻³
 - Vestibular signs¹⁻³
 - Nystagmus¹⁻³
 - Conscious proprioceptive deficits
 - Head tilt
 - Tremors
 - Seizures

Diagnosis & Treatment

- ⚠️ Administration of IV diazepam may be useful in definitive diagnosis of metronidazole toxicity, aiding in the transient, acute improvement in clinical signs.^{1,2,4}

- ⚠️ Immediate discontinuation of metronidazole, symptomatic and supportive care (eg, fluid therapy, antiemetic therapy), and diazepam therapy is advised.^{1,2,4}
 - Resolution can be seen within 14 days after drug therapy has been discontinued.²

- ⚠️ Diazepam therapy
 - **In dogs only**
 - Can decrease duration of clinical signs from 4.25 days in untreated dogs to 13.4 hours in treated dogs⁴
 - 0.43 mg/kg PO q8h for 3 days^{2,4}
 - **Warning for cats**
 - PO diazepam should not be used as treatment of metronidazole toxicity in cats because of risk for acute hepatic necrosis secondary to benzodiazepines.
 - IV administration can, however, be used to aid in the diagnosis of metronidazole toxicity.

High doses should be avoided in cats, as this species may be more sensitive to the effects of metronidazole.



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Clinical Polypharmacology Case



MANAGEMENT TREE

Drug Resistance Algorithm

A Glimpse of January!

- Controlling ventricular arrhythmias
- Ivermectin risks
- Pathogen profile
- Clinical case do's and don'ts
- Drug snapshot

REFERENCES

1. **Plumb's Veterinary Drug Handbook**, 7th ed. Plumb DC [ed]—Ames: Wiley-Blackwell, 2011, pp 682-685.
2. **Metronidazole**. Fitzgerald KT. In *Small Animal Toxicology*, 3rd ed—St. Louis: Saunders Elsevier, pp 653-658, 2013.
3. **Central nervous system toxicosis associated with metronidazole treatment of dogs: Five cases (1984-1987)**. Dow SW, LeCouteur RA, Poss ML, et al. *JAVMA* 195:365-368, 1989.
4. **Diazepam as a treatment for metronidazole toxicosis in dogs: A retrospective study of 21 cases**. Evans J, Levesque D, Knowles K, et al. *JVIM* 17:304-310, 2003.

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If signs of toxicity develop, immediately discontinue metronidazole treatment and begin symptomatic and supportive care, including fluid and antiemetic therapy.