

Therapeutic Drug Monitoring of Itraconazole in Dogs and Cats

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It is important to use generic or brand name (Sporanox) itraconazole, but not compounded itraconazole, for treatment of systemic infections such as blastomycosis and histoplasmosis. Generic and brand name itraconazole capsules contain “pelletized” drug with cyclodextrin, which improves solubility and enhances GI absorption of itraconazole, and both can produce comparable blood concentrations (1). Therapeutic concentrations are rarely achieved using the compounded powder formulation of itraconazole, which does not contain cyclodextrin and is poorly absorbed. Values may also be sub-therapeutic in 20-25% of patients receiving brand name or generic itraconazole. Blood levels by bioassay should ideally be in the range from 3.0 to 10.0 µg/mL. Results from 1.0-3.0 µg/mL are equivocal; however, results <1.0 µg/mL are definitely subtherapeutic and necessitate a dosage or medication change. Levels above 10 µg/mL may be associated with toxicity (2), are unnecessary, and justify dose reduction with reduced cost.

We have evaluated itraconazole blood levels in veterinary patients tested at MVD and found that levels were subtherapeutic (less than 3 µg/mL) in 98% of patients treated with a variety of compounded powder formulations (3; see Fig. 1). These compounded products had reportedly been acquired from numerous different sources. Subtherapeutic levels also occurred with generic (25%) and brand name (24%) itraconazole. Equally important is that potentially toxic levels were found in 38% of patients receiving the generic and 24% receiving brand name itraconazole.

A newer option for itraconazole in cats is Itrafungol suspension (Elanco). This product was unavailable at the time of our study, so it was not included in the “brand name” group. Itrafungol may be obtained at a much lower cost than Sporanox suspension or generic capsules, and the liquid form facilitates dosing in cats. This suspension does have a cherry-caramel flavor, so it may be unpalatable to some cats.

Itraconazole levels should be measured at steady state, typically 14 days (dogs) to 21 (cats) days after initiating therapy or changing the dose. As itraconazole has a long half-life, timing of the specimen after dosing is not critical but trough levels are preferred. The serum specimen should be frozen and shipped with a cold pack for next day delivery Monday through Friday to prevent degradation of the drug causing falsely-low levels.

Pharmacies with which we have experience that provide the pelletized form of itraconazole at reasonable prices include: Pet Apothecary in Wisconsin (<http://petapothecary.com/>; Dr. Jeff Langer, 414-247-8633) and Pet Health Pharmacy in Youngstown, Arizona (<http://www.pethealthpharmacy.com/>; Dr. Rich Gaffin 623-214-2791).

The itraconazole assay performed at MVD is a bioassay, as this method keeps the cost of testing low to allow for more patient monitoring. This method involves culturing of a *Candida* yeast and measurement of the zone of inhibition around the patient serum. Itraconazole concentration is estimated from a standard curve with samples containing known concentration of itraconazole. **Other antifungal drugs will interfere with the assay.** In patients receiving both terbinafine and itraconazole, or both fluconazole and itraconazole, measurement of itraconazole concentration by high performance liquid chromatography (HPLC) will be necessary.

Several options exist if the itraconazole blood level is low. First, if the patient is receiving compounded itraconazole, consider switching to generic or brand name itraconazole. If the cost of generic itraconazole is more than the owner can afford, the patient does not tolerate itraconazole, or levels of 3-10 µg/mL cannot be achieved, fluconazole, 10 mg/kg/day SID (dogs) or 10 mg/kg/day BID (cats) is an alternative. While fluconazole is not the treatment of choice for blastomycosis, and may be inferior to itraconazole, it is often used and a favorable outcome can be achieved in about 80% of cases with a six month course of fluconazole (4). Blood level monitoring is unnecessary when using fluconazole. Please feel free to call us at 866-647-2847 for a clinical consultation.

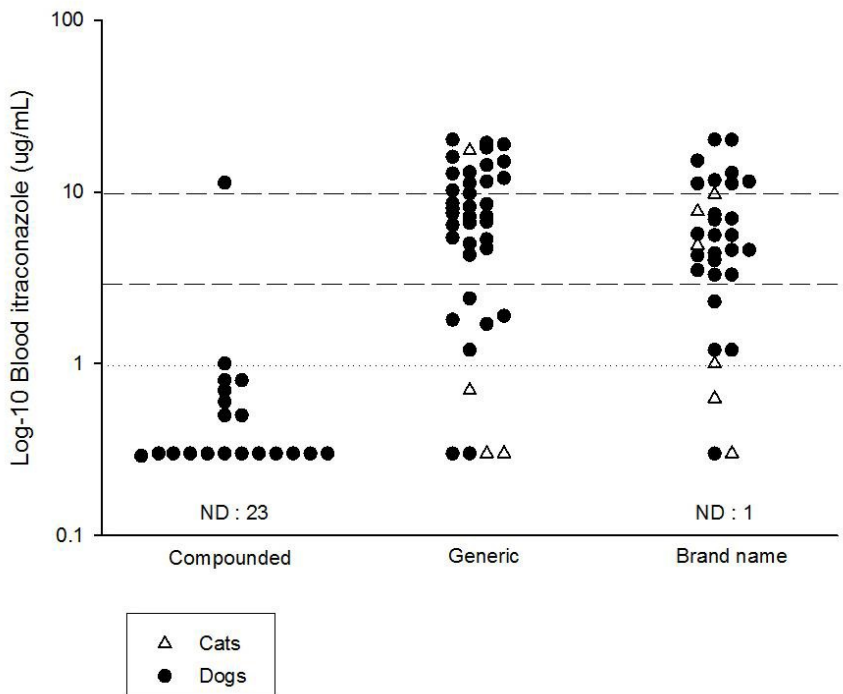


Figure 1. Distribution of blood itraconazole results for dogs and cats receiving compounded, generic or brand name itraconazole. Dashed lines indicate limits of therapeutic range (3-10 µg/mL) and dotted line indicates lower limit of equivocal range (1-2.9 µg/mL). ND=none detected.

References

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