



ITRACONAZOLE: How to Adjust Dose Based on MVista® Bioassay Result

At a Glance – Crucial Information

1. Itraconazole is an effective and commonly used antifungal drug
2. Adverse effects (AEs) are reported in 8-33% of dogs and cats treated [1-3]
3. AEs are more common with higher itraconazole blood levels
4. Treatment failure is more likely with sub-therapeutic blood levels
5. Blood levels are highly variable (both too high and low) even with appropriate dosing [4]
6. Therapeutic drug monitoring (TDM) of blood levels is recommended
7. TDM should be done after steady-state- 2 weeks in dogs and 3 weeks in cats
8. MVista® Itraconazole Bioassay is a cost-efficient option for TDM
9. MVista® Itraconazole Bioassay accounts for itraconazole and all active metabolites
10. Dose adjustment is simple using MVista® Itraconazole Bioassay results

Discussion

Itraconazole is one of the most commonly used antifungal drugs for invasive fungal infections (*Blasto*, *Histo*, *Cocci*, molds) in veterinary medicine. Itraconazole blood levels are highly variable from animal-to-animal [1,4-6]. At initial check, blood levels are commonly outside of the recommended therapeutic range, even with appropriate doses (Figure 1) [4]. Toxic levels often lead to adverse effects (AEs) including lethargy, anorexia, vomiting, diarrhea, hepatotoxicity, and ulcerative skin lesions [1]. Low levels are at least as common as toxic levels, which can cause treatment failure.

Therapeutic drug monitoring (itraconazole blood levels) is required to guide individualized care and minimize the risks of AEs and treatment failure. Blood levels should be checked after starting itraconazole and after each dosage change. The serum sample should be collected after reaching steady-state which is achieved within 3 weeks in cats and 2 weeks in dogs. If possible, the serum sample should be collected within 4 hours of the next dose (trough level). Table 1 provides an example of how to adjust dose based on the MVista® Bioassay. It assumes that drug levels have reached steady state and that the sample is near trough level.

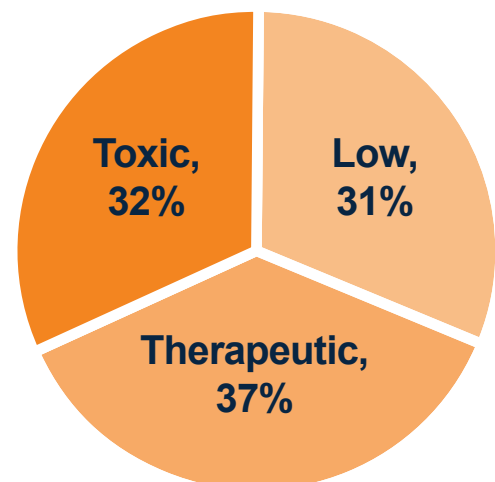


Figure 1. Itraconazole blood levels by MVista® Bioassay in 2000 consecutive samples from dogs and cats.

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CLINICAL TREATMENT & MONITORING

Itraconazole blood levels can be measured by different methods. The MVista® Bioassay uses the inhibition of fungal growth for this purpose. As compared with chromatography/spectrometry performed at pharmacology labs, the MVista® Bioassay provides significant cost-savings. In addition, the MVista® Bioassay, being a pharmacodynamic assay, accounts for itraconazole and all active metabolites. One disadvantage is that the administration of other antifungal drugs can lead to falsely high results. As such, other antifungals should be discontinued 1 week before drawing sample for MVista® Bioassay.

Table 1. Daily dose adjustment based on MVista® Bioassay itraconazole blood level.

Itraconazole blood level (mcg/ml)	Adjustment (to dose daily)	Notes
<2	Double	Recheck in 3 weeks.
2-7	No change	Recheck in 6 months, or sooner if indicated.
7-10 (NO adverse effects)	No change	Normal or improving appetite and Normal ALT. Recheck in 6 months, or sooner if indicated.
7-10 (adverse effects present)	Decrease 25-50%	Decreased appetite, GI signs, or Increasing ALT. Recheck in 3 weeks.
>10	Half	Recheck in 3 weeks.

Recommendations assume blood levels have reached steady-state (2 weeks in dogs; 3 weeks in cats) and are near trough (within 4 hours of next dose).

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