



Histoplasmosis: When to Stop Antifungal Treatment

At a Glance – Crucial Information

1. MVista® *Histoplasma* Antigen test can be used for diagnosis, treatment monitoring, and detection of disease relapse.
2. Treatment monitoring includes following clinical signs, physical exam findings, imaging study results, and antigen concentrations.
3. Antigen concentrations decrease with effective treatment and increase with disease relapse.
4. MVista® *Histo* Antigen test should be performed at diagnosis, every 3 months during treatment, and at 6 months then every 12 months after treatment.

The MVista® *Histoplasma* Antigen test has revolutionized diagnosis and treatment monitoring of histoplasmosis. It provides a non-invasive option with high diagnostic performance (sensitivity = 93%, specificity = 98%) [1-4]. With effective treatment, antigen concentrations decrease [5]. With ineffective treatment or disease relapse, antigen concentrations remain static or increase over time [5]. Many dogs and most cats have no detectable antigen at the time of disease remission [5]. Less frequently, a very low concentration of antigen is present, even after remission. In these cases, it might be appropriate to stop treatment even when the antigen test is still positive (**Table 1**).

Urine is the ideal sample when using the MVista® *Histoplasma* Antigen test for treatment monitoring. It commonly contains a higher antigen concentration, as compared with serum, and thus is a better marker for remission and relapse [5]. When urine antigen concentration is too high to be quantified (above the limit of quantification), serum can often be used instead until urine concentrations are quantifiable. In these cases, urine antigen is often quantifiable at the 6 months recheck.

Disease relapse has been reported in approximately 20-40% of dogs and cats treated for histoplasmosis [5, 6]. Intuitively, a treatment duration that is too short increases the chance of disease relapse. A multimodal monitoring approach helps guide appropriate individualized treatment duration (**Table 1**). In addition, appropriate drug and dosage are vital. Itraconazole is the first-choice treatment for animals not hospitalized. Due to variability in absorption, itraconazole blood levels should be monitored to determine the ideal individualized dose. This can be achieved with the MVista® Itraconazole Bioassay, which accounts for parent drug and all active metabolites. It has the additional advantage of being significantly less expensive than chromatography/spectrometry testing available from pharmacology labs. The bioassay is affected by antifungal drugs other than itraconazole and these should be discontinued at least 1 week before checking itraconazole blood levels. Ideally, the sample should be drawn within 4 hours of the next dose (near-trough) and after at least 3 weeks of therapy to allow blood levels to reach steady-state.

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CLINICAL TREATMENT & MONITORING

Table 1. All of the following criteria should be met before stopping antifungal treatment in dogs and cats with histoplasmosis.

Monitoring Tool	Criteria	Notes
Treatment Duration	Minimum of 6 months	<ul style="list-style-type: none"> Required duration is often much longer.
History	≥1-month past resolution of clinical signs	<ul style="list-style-type: none"> Mild exercise intolerance might persist, most notable in working or performance animals. Persistent tracheobronchial lymphadenopathy can cause cough, requiring concurrent corticosteroid treatment.
Physical Examination	≥1-month past resolution of physical exam abnormalities	<ul style="list-style-type: none"> Differentiating active ocular disease from permanent inactive change is important.
Imaging Studies	≥1-month past resolution of imaging abnormalities	<ul style="list-style-type: none"> Pulmonary scarring can be permanent and can cause static focal unstructured interstitial lung disease. Radiographic bone lesions should improve but might never return to normal.
MVista® <i>Histoplasma</i> Antigen EIA (urine)	≥1-month past no detectable antigen OR Antigen ≤0.4 ng/ml on 2 consecutive rechecks at least 3 months apart	<ul style="list-style-type: none"> Most dogs, and essentially all cats, have no detectable antigen at the time of remission. Submit antigen test at diagnosis, every 3 months during treatment, and at 6 months then every 12 months after treatment.

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