Malassezia pachydermatis William Oldenhoff, DVM, DACVD Pittsburgh Veterinary Specialty & Emergency Center Pittsburgh, Pennsylvania

Malassezia pachydermatis infection is frequently undiagnosed, as making a diagnosis is often difficult when clinical signs overlap a number of other clinical conditions (eg, atopic dermatitis, seborrhea). In addition, there are no consistently effective quantitative cytology techniques.

Response-to-treatment trials are an important component in diagnosing *Malassezia* spp dermatitis.^{1,2} Treatment should be considered when yeast has been identified on cytology in a patient showing clinical signs compatible with *Malassezia* spp dermatitis. Recurrent *M pachydermatis* overgrowth is common and often secondary to underlying conditions (eg, allergies, seborrhea, endocrinopathies, skinfolds).

In addition to acute management of infection, treatment success relies on appropriate diagnosis and management of predisposing conditions.

SYSTEMIC THERAPY

Ketoconazole

Dogs: 5-10 mg/kg PO once a day for 2-4 weeks¹⁻³

Cats: Not recommended because of high incidence of side

effects1,2

Ketoconazole, an imidazole antifungal, impairs ergosterol synthesis in fungal cell walls by inhibiting cytochrome P450 14 α -demethylase (CYP51). Ketoconazole has efficacy against a wide range of fungal organisms and has been shown to have anti-inflammatory effects.⁴

Most commonly used systemic treatment for dermatitis caused by M pachydermatis in dogs⁴

Itraconazole

Dogs: Daily treatment, 5-10 mg/kg PO once a day for 2-4 weeks¹⁻³; pulse treatment, 5-10 mg/kg PO for the first 2 days of each week^{2,5}

Cats: 5-10 mg/kg PO once a day for 2-4 weeks^{1,2}

Itraconazole, a triazole antifungal, inhibits CYP51, resulting in impaired ergosterol synthesis in fungal cell walls. ^{1,2,5} Itraconazole is lipophilic and highly protein-bound, and therapeutic levels persist in the skin days to weeks after treatment is stopped. ^{1,2,5} This principle likely explains why pulse treatment appears to be effective. ⁵

Fluconazole

Dogs: 5-10 mg/kg PO once a day for 2-4 weeks^{1,2,6,7}

Although many topical products are available for treating *Malassezia* spp dermatitis, only a few controlled studies have documented efficacy.^{3,11}

Cats: Fluconazole treatment of *M pachydermatis* infections in cats has not been studied.

Like itraconazole, fluconazole is a triazole antifungal that impairs ergosterol synthesis in fungal cell walls via inhibition of CYP51. 1,2,6,7 Fluconazole is comparable in efficacy to ketoconazole in treating *Malassezia* spp dermatitis in dogs. 6

Terbinafine

Dogs: 30 mg/kg PO once a day 8,9 or 30 mg/kg PO for 2 consecutive days each week for 3-4 weeks 10

Cats: Terbinafine treatment of *M pachydermatis* infections in cats has not been studied.

Terbinafine, an allylamine antifungal drug, inhibits ergosterol synthesis and squalene epoxidase, resulting in ergosterol deficiency and squalene accumulation in fungal cell walls. It does not inhibit cytochrome P450 enzymes. Although terbinafine has been shown to reduce *M pachydermatis* populations and dermatitis in dogs treated for 3 weeks, longer durations of therapy or adjunctive use of topical agents may be necessary to achieve resolution.^{8,9,10}

Griseofulvin

Dogs, cats: Not recommended for use in dogs or cats^{1,2}

Griseofulvin inhibits cell mitosis and nucleic acid synthesis in fungal organisms by interfering with spindle microtubules. However, this agent is not effective in treating *Malassezia* spp dermatitis in dogs or cats.

CYP51 = cytochrome P450 14 α -demethylase

TOPICAL THERAPY

Antifungal Shampoos

Dogs, cats: Some topical products supported by clinical evidence^{3,11}

- ► Strong evidence supports twice-weekly use of 2% miconazole + 2% chlorhexidine shampoo.³
 - For both dogs and cats, including puppies and kittens
- Once- or twice-daily application of 0.3% chlorhexidine + 0.5% climbazole and Tris-EDTA wipe has been shown to reduce M pachydermatis populations in naturally infected dogs.¹¹
 - For dogs only
 - May also be effective in dogs with localized overgrowth of M pachydermatis

Antifungal shampoos can be an important component in treating *Malassezia* spp dermatitis. For mild-to-moderate or localized infections, they may be the sole therapy. For generalized or severe infections, topical therapy should be combined with systemic therapy.

- ► Although many topical products are available for treating Malassezia spp dermatitis, only a few controlled studies have documented efficacy.^{3,11}
- ► Further studies are needed to evaluate other topical products. ■

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References

- Bond R. Cutaneous fungal infections: Malassezia dermatitis. In: Greene CE, ed. Infectious Diseases of the Dog and Cat. 4th ed. St. Louis, MO: Elsevier Health Sciences; 2013:602-606.
- Miller WH, Griffin CE, Campbell KL. Fungal and algal skin diseases: Malassezia dermatitis. In: Miller WH, Griffin CE, Campbell KL, eds. Muller and Kirk's Small Animal Dermatology. 7th ed. St. Louis, MO: Elsevier Health Sciences: 2013:243-249.
- 3. Negre A, Bensignor E, Guillot J. Evidence-based veterinary dermatology:

- a systematic review of interventions for *Malassezia* dermatitis in dogs. *Vet Dermatol.* 2009;20(1):1-12.
- Van Cutsem J, Van Gerven F, Cauwenbergh G, Odds F, Janssen PA. The antiinflammatory effects of ketoconazole: a comparative study with hydrocortisone acetate in a model using living and killed Staphylococcus aureus on the skin of guinea pigs. J Am Acad Dermatol. 1991;25(2 Pt 1):257-261.
- Pinchbeck LR, Hillier A, Kowalski JJ, Kwochka KW. Comparison of pulse administration versus once daily administration of itraconazole for the treatment of Malassezia pachydermatis dermatitis and otitis in dogs. JAVMA. 2002:220(12)1807-1812.
- Sickafoose L, Hosgood G, Snook T, Westermeyer R, Merchant S. A noninferiority clinical trial comparing fluconazole and ketoconazole in combination with cephalexin for the treatment of dogs with *Malassezia* dermatitis. Vet Ther. 2010:11(2):E1-13.
- Jesus FP, Lautert C, Zanette RA, et al. In vitro susceptibility of fluconazole-susceptible and resistant isolates of Malassezia pachydermatis

- against azoles. *Vet Microbiol*. 2011;152(1-2):161-164.
- Guillot J, Bensignor E, Jankowski F, Seewald W, Chermette R, Steffan R. Comparative efficacies of oral ketoconazole and terbinafine for reducing *Malassezia* population sizes on the skin of basset hounds. *Vet Dermatol*. 2003;14(3):153-157.
- Rosales MS, Marsella R, Kunkle G, Harris BL, Nicklin CF, Lopez J. Comparison of the clinical efficacy of oral terbinafine and ketoconazole combined with cephalexin in the treatment of Malassezia dermatitis in dogs—a pilot study. Vet Dermatol. 2005;16(3):171-176.
- Berger DL, Lewis TP, Schick AE, Stone RF. Comparison of once-daily versus twice-weekly terbinafine administration for the treatment of canine Malassezia dermatitis—a pilot study. Vet Dermatol. 2012;23(5):418-e79.
- Cavana P, Peano A, Petit JY, et al. A pilot study of the efficacy of wipes containing chlorhexidine 0.3%, climbazole 0.5% and Tris-EDTA to reduce Malassezia pachydermatis populations on canine skin. Vet Dermatol. 2015;26(4):278-e61.

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- Klein HE, Krohne SG, Moore GE, Stiles J. Postoperative complications and visual outcomes of phacoemulsification in 103 dogs (179 eyes): 2005-2008. Vet Ophthalmol. 2011;14(2):114-120.
- Schmidt GM, Vainisi SJ. Retrospective study of prophylactic random transscleral retinopexy in the Bichon Frise with cataract. Vet Ophthalmol. 2004;7(5):307-310.
- Moeller E, Blocker T, Esson D, Madsen R. Postoperative glaucoma in the Labrador Retriever: incidence, risk factors, and visual outcome following routine phacoemulsification. Vet Ophthalmol. 2011;14(6):385-394.

Suggested Reading

Gelatt KN. Surgery of the lens. In: Gelatt KN, Gilger BC, Kern TJ. *Veterinary Ophthalmology*. 5th ed. Ames, IA: John Wiley & Sons; 2013:1234-1286.

Meloxidyl® (meloxicam)

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(meloxicam) 1.5 mg/mL Oral Suspension

Non-steroidal anti-inflammatory drug for oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Indications: Meloxidyl Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Contraindications: Dogs with known hypersensitivity to meloxicam should not receive Meloxidyl Oral Suspension. Do not use Meloxidyl Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.

Warning: Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information.

Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. For oral use in dogs only.

As with any NSAID, all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration. Owner should be advised to observe their dog for signs of potential drug toxicity and be given a client information sheet about Meloxxfyl Oral Suspension.

Precautions: The safe use of Meloxidyl Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating dogs has not been evaluated. Meloxicam Oral Suspension is not recommended for use in dogs with bleeding disorders, as easfely has not been established in dogs with these disorders. As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from one PSAID may inhibit the prostagland in the maintain normal homeostatic function. Such antiprostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after administration of the total daily dose of Meloxidyl Oral Suspension, a non-NSAID or non-corticosteroid class of analgesia should be considered. The use of anonther NSAID is not recommended. Consider appropriate washout times when switching from corticosteroid use or from one NSAID to another in dogs. The use of concomitantly protein-bound drugs with Meloxyl Oral Suspension has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit medications in finitioner in patients requiring adjunctive therapy.

Adverse Reactions: Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft shots), diarrhea, and inappetance) were the most common adverse reactions associated with the administration of meloxicam. The following table lists adverse reactions and the numbers of dogs that experienced them during the studies. Dogs may hav experienced more than one episode of the adverse reaction during the studies.

In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to melou/cam administration included: auto-immune hemolytic anemia (1 dog), thrombocylopenia (1 dog), polyarthritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).

Adverse Reactions Observed During Two Field Studies		
Clinical Observation	Meloxicam (n+157)	Placebo (n+149)
Vomiting	40	23
Dianhea/Soft Stool	19	- 11
Bloody Stool	1	0
Inappetence	5	1
Bleeding Gums After Dental Procedure	1	0
Lethargy/Swollen Carpus	1	0
Eniphora	1	0

Post-Approval Experience: (Rev 2010)

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system.

Gastrointestinal: vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration

Urinary: azotemia, elevated creatinine, renal failure Neurological/Behavioral: lethargy, depression Hepatic: elevated liver enzymes

Dermatologic: pruritus

Death has been reported as an outcome of the adverse events listed above. Acute renal failure and death have been associated with use of meloxicam in cats.

meloxicam in cats.

Effectiveness: The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, betweens six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In the first field study (n= 109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n = 48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters, however, statistical significance was demonstrated only for the overall investigator evaluation on day 14.

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