

# Oral Metronidazole Therapeutic Cheat Sheet

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## TRADE NAME

- › Flagyl

## MECHANISM OF ACTION

- › Metronidazole is an oral nitroimidazole. Nitroimidazoles are prodrugs which enter organisms and are reduced in the presence of low oxygen tension, leading to fragmentation of imidazole and cytotoxicity. The mechanism of action is not entirely clear, but is thought that imidazole metabolites interact and disrupt DNA helices, leading to inhibition of nucleic acid synthesis.<sup>1</sup>

## FDA APPROVED USES

- › To treat protozoan and anaerobic bacterial infections

## OFF-LABEL USES IN DERMATOLOGY

- › Rosacea (including granulomatous rosacea)
- › Oral and cutaneous lichen planus
- › Hidradenitis suppurativa
- › Periorificial dermatitis
- › Demodicosis
- › Tropical ulcers
- › Cutaneous metastatic Crohn disease<sup>2</sup>
- › Granulomatous cheilitis<sup>3</sup>
- › Lupus miliaris disseminatus faciei (LMDF)<sup>4</sup>
- › Eosinophilic pustular folliculitis<sup>5</sup>

## DERMATOLOGIC DOSING

- › The most commonly reported dosage of oral metronidazole used in dermatology for adults is 500mg twice daily. However, some authors have reported success in lichen planus and demodicosis at a dose of 250mg every 8 hours<sup>6,7</sup> and in LMDF at an even lower dose of 250mg BID<sup>4</sup>

## SAFETY MONITORING

- › CBC at baseline and throughout treatment is recommended in the case of prolonged treatment courses. Patients should be closely monitored for the development of neurotoxicity. Close monitoring is also recommended in patients with hepatic and renal disease.<sup>10</sup>

## SIDE EFFECTS

- › Disulfiram-like reaction when consumed with alcohol
- › Abdominal pain
- › Diarrhea
- › Metallic taste
- › Headache
- › Dizziness
- › Vaginitis
- › Hepatotoxicity, in the setting of Cockayne syndrome
- › Neurotoxicity may occur, especially in the setting of prolonged treatment courses as the risk may be cumulative. This may present as peripheral neuropathy, encephalopathy, altered mental status, ataxia, optic neuropathy and seizures.<sup>8</sup>
- › Prolonged use may increase risk of certain fungal and bacterial infections, including candidiasis and *C difficile* infection with associated pseudomembranous colitis
- › Rare reports of transient leukopenia, neutropenia and thrombocytopenia<sup>9</sup>
- › Cutaneous adverse reactions have been reported and include Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), and drug-induced hypersensitivity syndrome (DIHS)
- › There is a black box warning of carcinogenicity based on animal studies, however, treatment in humans does not appear to increase cancer risk

## CONTRAINDICATIONS

- › Hypersensitivity to drug component
- › Concomitant alcohol use. It is recommended patients avoid alcohol during treatment and for two additional weeks following treatment
- › Disulfiram use
- › Cockayne syndrome
- › Caution if: hepatic impairment, electrolyte abnormalities, recent myocardial infarction, congestive heart failure, bradycardia, certain arrhythmias such as those involving QT prolongation

## PREGNANCY

- › Contraindicated in the first trimester of pregnancy, as there have been rare reports of teratogenicity including cleft lip and palate. During lactation, milk drug level concentrations are similar to maternal serum concentrations. Therefore, a risk benefit analysis should be performed given the theoretical risk of tumorigenicity based on animal models.<sup>10</sup>
- › Oral metronidazole is frequently used off-label for various inflammatory dermatologic disorders. It is generally well tolerated and therefore a safe and efficacious alternative in our therapeutic arsenal.