

Clotrimazole

Antifungal Class:

Azoles (specifically imidazole)

Antimicrobial Spectrum:

Fungi: *Blastomyces dermatitidis*, *Candida* spp, *Coccidioides immitis*, *Cryptococcus neoformans*, Dermatophytes (Trichophyton, Microsporum, Epidermophyton), *Histoplasma capsulatum*, *Malassezia furfur*, *Naegleria fowleri*, *Nocardia* spp, *Paracoccidioides brasiliensis*, *Sporotrichum schenckii*

Mechanism of Action:

Bind to the heme moiety of the fungal cytochrome P-450 dependent enzyme lanosterol 14- α -demethylase. Inhibits 14- α -demethylase, blocks formation of ergosterol and leads to the buildup of toxic methylated 14- α -sterols. Both effects serve to inhibit cell growth.

Pharmacodynamics:

Other azoles have shown in murine models to exhibit AUC:MIC ratio as predictive of effect for *Candida* spp. This may vary by fungal species however.

Pharmacokinetics:

Absorption: Topical: negligible through intact skin

Time to peak, serum:

Oral, topical: Salivary levels occur within 3 hours after 30 minutes of dissolution time

Vaginal cream: High vaginal levels: 8-24 hours.

Excretion: Feces (as metabolites)

Adverse Effects:

Oral tablets:

Gastrointestinal: nausea, vomiting

Vaginal:

Genitourinary: vaginal/vulvar bleeding

Burning or itching of penis of sexual partner; polyuria; vulvar itching, soreness, edema, discharge.

Dosage:

Cream, topical: 1% (15g, 30g, 45g, 90g)

Cream, vaginal: 1% (45g, 90g), 2% (25g)

Lotion: 1% (30 mL)

Solution, topical: 1% (10 mL, 30 mL)

Tablet, vaginal: 100mg, 200mg, 500mg

Troche: 10mg

Adults and children > 3 years:

Troche: 10 mg troche dissolved 5 times/day for 14 days.

Adults and children > 12 years:

Vaginal cream 1%: Insert 1 applicatorful daily (preferably at bedtime) for 7 – 14 days.

2%: Insert 1 applicatorful daily (preferably at bedtime) for 3 consecutive days.

Vaginal tablets: Insert 100 mg/day for 7 days or 500 mg single dose.

Topical: Apply to affected area twice daily (morning and evening).

Disease state based dosing:

Renal failure: No dosing adjustment necessary

Hepatic failure: No dosing adjustment necessary

Contraindications/Warnings/Precautions:

Precautions: Clotrimazole should not be used for treatment of systemic fungal infection

Drug Interactions:

Clotrimazole is an inhibitor of the cytochrome P450 3A4, 2A6, 2C8/9, and 2E1 isoenzymes. Caution should be exercised and monitoring is suggested when concomitantly administering clotrimazole with drugs that have narrow therapeutic windows and are substrates of aforementioned CYP substrates.

Table 4

Pregnancy:

Topical: Category B: No evidence of risk in humans but studies inadequate.

Troches: Category C: Risk unknown. Human studies inadequate.

Monitoring Requirements:

Consider periodic liver function tests during prolonged oral therapy with clotrimazole lozenges.

Brand names/Manufacturer:

Available by many names and manufacturers