NEXTSTEPS IN DERM | GW School of Medicine & Health Sciences

Fluconazole Therapeutic Cheat Sheet

COMPILED BY: NAGASAI ADUSUMILLI, MD, MBA | REVIEWED BY: ADAM FRIEDMAN, MD, FAAD

TRADE NAME

- Diflucan

MECHANISM OF ACTION

- As a triazole, fluconazole inhibits the enzyme lanosterol 14α demethylase, blocking the conversion of lanosterol to ergosterol in fungal cell membranes and resulting in a fungistatic action.

FDA-APPROVED FOR

- Vaginal, oropharyngeal, and esophageal candidiasis
- Systemic *Candida* infections, including candidemia, disseminated candidiasis, pneumonia
- Cryptococcal meningitis
- Prophylaxis against candidiasis during bone marrow transplant and associated cytotoxic chemotherapy or radiation therapy

OFF-LABEL DERMATOLOGIC USES[1-6]

- Blastomycosis
- Candidal intertrigo
- Coccidiomycosis
- Cryptococcosis
- Histoplasmosis
- Leishmaniasis
- Onychomycosis
- Paracoccidioidomycosis
- Sporotrichosis
- Talaromycosis
- *Tinea capitis, corporis, cruris, pedis, manuum*
- *Tinea versicolor*

ADULT ORAL DOSING (UNLESS SPECIFIED)

- Blastomycosis, coccidiomycosis
  - Oral 400 – 800 mg once daily for 6 – 12 months[2,3]
- Candidal intertrigo
  - Oral 150 mg once weekly for 4 weeks[7]
- Cryptococcosis, disseminated, nonmeningeal
  - Oral 400 – 800 mg once daily for 10 weeks, followed by oral 200 mg once daily for a total of 6 months[4]
- Histoplasmosis
  - Oral 800 mg once daily for 12 months[4]
  - Secondary prophylaxis with severe disseminated disease and relapse despite appropriate initial therapy: oral 400 mg once daily[4]
- Leishmaniasis
  - Oral 200 mg once daily for 6 weeks[6]
  - For L. major, oral 400 mg once daily for 6 weeks[6]
- Onychomycosis
  - Oral 150 – 450 mg once weekly for 3 months (fingernail) or 6 – 12 months (toenail)[5]
- Sporotrichosis
  - Oral 400 – 800 mg once daily for 4 weeks after lesion resolution, typically around 3 – 6 months
- Talaromycosis
  - Primary prophylaxis in patients with HIV, with CD4 count <100 cells/mm^3, in highly endemic regions (northern Thailand, Vietnam, southern China)[4]
  - Oral 400 mg once weekly until CD4 count >100 cells/mm^3
- Tinea capitis
  - Pediatric: Oral 6 mg/kg/dose (Max: 400 mg/dose) once daily for 3 – 6 weeks[8]
- Tinea corporis, cruris
  - Oral 150 – 200 mg once weekly for 2 – 4 weeks[9]
- Tinea pedis, manuum
  - Oral 150 – 200 mg once weekly for 2 – 6 weeks[9]
- Tinea versicolor
  - Oral 300 mg once weekly for 2 weeks[10]
- Oropharyngeal candidiasis
  - For moderate to severe disease with poor response to topical treatment or with recurrent infection, 200 mg once, then 100 – 200 mg once daily for 1 – 2 weeks[1]
- Vulvovaginal candidiasis
  - If immunocompetent, oral 150 mg once as single dose[1]
  - If immunocompromised, oral 150 mg once every 3 days for 3 doses[1]
  - If recurrent, oral 150 mg once every 3 days for 3 doses, then oral 150 mg once weekly for 6 months[11]

ADMINISTRATION CONSIDERATIONS[12]

- Oral suspension formulation contains sucrose and should be avoided in patients with rare hereditary fructose metabolism conditions.
- Oral capsules contain lactose and should be avoided in patients with rare hereditary galactose metabolism conditions.
- Caution should be used in the setting of liver dysfunction due to fluconazole-associated hepatotoxicity.
- Caution should be used with coadministration of other QTc prolonging agents, especially in patients with baseline QTc prolongation or history of torsades de pointes.

SIDE EFFECTS[13]

- Nausea, headache, vomiting, and abdominal pain are the most frequently reported in clinical trials.
- Limited case reports of Stevens-Johnson syndrome, toxic epidermal necrolysis, angioedema, and erythema multiforme

DRUG INTERACTIONS[12]

- Moderate CYP3A4 and CYP2C9 inhibitor. Systemic medications metabolized by these substrates include, but are not limited to, quinidine, pimozide, erythromycin, and astemizole (QTc prolongation); atorvastatin, simvastatin, and fluvastatin (rhabdomyolysis); sulfonylureas (hypoglycemia); tacrolimus (nephrotoxicity).

CONTRAINDICATIONS[12]

- History of anaphylaxis or hypersensitivity to fluconazole
- If using multiple doses of 400mg or higher, fluconazole is contraindicated for coadministration with terfenadine.
- Coadministration with CYP3A4 and CYP2C9 substrates can lead to QTc prolongation.

PREGNANCY AND BREASTFEEDING[12]

- Limited studies of fluconazole use in pregnant women. Limited case reports of birth defects with 400-800 mg/day doses.
- Category D, should not be used if pregnant, planning a pregnancy, or breastfeeding

MONITORING

- Baseline Labs:
  - Liver enzymes in patients with preexisting liver disease
- Periodic monitoring:
  - Liver enzymes if signs and symptoms of hepatic injury or if requiring multiple doses of at least 400mg

REFERENCES

1. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016 Feb 15:62(4):e1-50.
2. Galgiani JN, Ampel NM, Blair JE, et al. 2016 Infectious Diseases Society of America (IDSA) clinical practice guideline for the treatment of coccidioidomycosis. Clin Infect Dis. 2016 Sep 15:63(6):e112-46.
3. Chapman SW, Dismukes WE, Proia LA, et al; Infectious Diseases Society of America. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. Clin Infect Dis. 2008 Jun 15:46(12):1801-12.
4. Kaplan JE, Benson C, Holmes K et al; Centers for Disease Control and Prevention (CDC); National Institutes of Health; HIV Medicine Association of the Infectious Diseases Society of America. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep. 2009 Apr 10:58(RR-4):1-207.
5. Ameen M, Lear JT, Madan V, Mohd Mustapa MF, Richardson M. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. Br J Dermatol. 2014 Nov:171(5):937-58.
6. Stevens DL, Bisno AL, Chambers HF, et al; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15:59(2):e10-52.
7. Nozickova M, Koudelkova V, Kulikova Z, et al. A comparison of the efficacy of oral fluconazole, 150 mg/week versus 50 mg/day, in the treatment of tinea corporis, tinea cruris, tinea pedis, and cutaneous candidosis. Int J Dermatol. 1998 Sep:37(9):703-5.
8. Gupta AK, Mays RR, Versteeg SG, et al. Tinea capitis in children: a systematic review of management. J Eur Acad Dermatol Venereol. 2018 Dec;32(12):2264-2274.
9. Montero-Gei F, Perera A. Therapy with fluconazole for tinea corporis, tinea cruris, and tinea pedis. Clin Infect Dis. 1992 Mar;14 Suppl 1:S77-81.
10. Gupta AK, Lane D, Paquet M. Systematic review of systemic treatments for tinea versicolor and evidence-based dosing regimen recommendations. J Cutan Med Surg. 2014 Mar-Apr;18(2):79-90.
11. Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep. 2021 Jul 23;70(4):1-187.
12. Pfizer Inc. Diflucan fluconazole tablets; fluconazole for oral suspension (prescribing information). Revised February 2019. Available at http://labeling.pfizer.com/ShowLabeling.aspx?id=575 . Accessed Oct 20, 2023.
13. Stevens DA, Diaz M, Negroni R, et al. Safety evaluation of chronic fluconazole therapy. Fluconazole Pan-American Study Group. Chemotherapy. 1997 Sep-Oct;43(5):371-7.