Fluconazole:

Class: Antifungal.

Indications:

Treatment of candidiasis (esophageal, oropharyngeal, peritoneal, urinary tract, vaginal); systemic candida infections (eg, candidemia, disseminated candidiasis, and pneumonia); cryptococcal meningitis; antifungal prophylaxis in allogeneic bone marrow transplant recipients.

Available dosage form in the hospital: 2MG/ML VIAL, 150MG CAP, 50MG CAP.

Trade Names:

Dosage:

Usual dosage range: Oral, I.V: 150 mg once **or** Loading dose: 200-800 mg; maintenance: 200-800 mg once daily; duration and dosage depend on location and severity of infection

Indication-specific dosing:

Blastomycosis (unlabeled use): Oral: *CNS disease:* Consolidation: 800 mg daily for ≥12 months and until resolution of CSF abnormalities (Chapman, 2008)

Candidiasis: Oral, I.V.:

Candidemia (neutropenic and non-neutropenic): Loading dose: 800 mg (12 mg/kg) on day 1, then 400 mg daily (6 mg/kg/day) for 14 days after first negative blood culture and resolution of signs/symptoms. **Note:** Not recommended for patients with recent azole exposure, critical illness, or if *C. krusei* or *C. glabrata* are suspected (Pappas, 2009).

Chronic, disseminated: 400 mg daily (6 mg/kg/day) until calcification or lesion resolution (Pappas, 2009)

CNS candidiasis (alternative therapy): 400-800 mg daily (6-12 mg/kg/day) until CSF/radiological abnormalities resolved. **Note:** Recommended as alternative therapy in patients intolerant of amphotericin B (Pappas, 2009).

Endocarditis, prosthetic valve (unlabeled use): 400-800 mg daily (6-12 mg/kg/day) for 6 weeks after valve replacement (as step-down in stable, culture-negative patients); long-term suppression in absence of valve replacement: 400-800 mg daily (Pappas, 2009)

Endophthalmitis (unlabeled use): 400-800 mg daily (6-12 mg/kg/day) for 4-6 weeks until examination indicates resolution (Pappas, 2009)

Esophageal:

Manufacturer's recommendation: Loading dose: 200 mg on day 1, then maintenance dose of 100-400 mg daily for 21 days and for at least 2 weeks following resolution of symptoms

Alternative dosing: 200-400 mg daily for 14-21 days; suppressive therapy of 100-200 mg 3 times weekly may be used for recurrent infections (Pappas, 2009)

Intertrigo (unlabeled use): 50 mg daily or 150 mg once weekly (Coldiron, 1991; Nozickova, 1998; Stengel, 1994)

Oropharyngeal:

Manufacturer's recommendation: Loading dose: 200 mg on day 1; maintenance dose 100 mg daily for ≥2 weeks. **Note:** Therapy with 100 mg daily is associated with resistance development (Rex, 1995).

Alternative dosing: 100-200 mg daily for 7-14 days for uncomplicated, moderate-to-severe disease; chronic therapy of 100 mg 3 times weekly is recommended in immunocompromised patients with history of oropharyngeal candidiasis (OPC) (Pappas, 2009)

Osteoarticular: 400 mg daily for 6-12 months (osteomyelitis) or 6 weeks (septic arthritis) (Pappas, 2009)

Pacemaker (or ICD, VAD) infection (unlabeled use): 400-800 mg daily (6-12 mg/kg/day) for 4- 6 weeks after device removal (as step-down in stable, culture-negative patients); long-term suppression when VAD cannot be removed: 400-800 mg daily (Pappas, 2009)

Pericarditis or myocarditis: 400-800 mg daily for several months (Pappas, 2009)

Peritonitis: 50-200 mg daily. **Note:** Some clinicians do not recommend using <200 mg daily (Chen, 2004).

Prophylaxis:

Bone marrow transplant: 400 mg once daily. Patients anticipated to have severe granulocytopenia should start therapy several days prior to the anticipated onset of neutropenia and continue for 7 days after the neutrophil count is >1000 mm^3.

High-risk ICU patients in units with high incidence of invasive candidiasis: 400 mg once daily (Pappas, 2009)

Neutropenic patients: 400 mg once daily for duration of neutropenia (Pappas, 2009)

Peritoneal dialysis associated infection (concurrently treated with antibiotics), prevention of secondary fungal infection: 200 mg every 48 hours (Restrepo, 2010)

Solid organ transplant: 200-400 mg once daily for at least 7-14 days (Pappas, 2009)

Thrombophlebitis, suppurative (unlabeled use): 400-800 mg daily (6-12 mg/kg/day) and as step-down in stable patients for ≥2 weeks (Pappas, 2009)

Urinary tract:

Cystitis:

Manufacturer's recommendation: UTI: 50-200 mg once daily

Asymptomatic, patient undergoing urologic procedure: 200-400 mg once daily several days before and after the procedure (Pappas, 2009)

Symptomatic: 200 mg once daily for 2 weeks (Pappas, 2009)

Fungus balls: 200-400 mg once daily (Pappas, 2009)

Pyelonephritis: 200-400 mg once daily for 2 weeks (Pappas, 2009)

Vaginal:

Uncomplicated: Manufacturer's recommendation: 150 mg as a single oral dose

Complicated: 150 mg every 72 hours for 3 doses (Pappas, 2009)

Recurrent: 150 mg once daily for 10-14 days, followed by 150 mg once weekly for 6 months (Pappas, 2009), **or** fluconazole (oral) 100 mg, 150 mg, or 200 mg every third day for a total of 3 doses (day 1, 4, and 7), then 100 mg, 150 mg, or 200 mg dose weekly for 6 months (CDC, 2010)

Coccidioidomycosis, treatment: Oral, I.V.:

HIV-infected (unlabeled use):

Meningitis: 400-800 mg once daily continued indefinitely (CDC, 2009)

Pneumonia, focal, mild or positive serology alone: 400 mg once daily continued indefinitely (CDC, 2009)

Pneumonia, diffuse or severe extrathoracic disseminated disease (after clinical improvement noted with amphotericin B): 400 mg once daily (CDC, 2009)

Non-HIV infected (unlabeled use):

Disseminated, extrapulmonary: 400 mg once daily (some experts use 2000 mg daily [Galgiani, 2005])

Meningitis: 400 mg once daily (some experts use initial doses of 800-1000 mg daily), lifelong duration (Galgiani, 2005)

Pneumonia, acute, uncomplicated: 200-400 mg daily for 3-6 months (Catanzaro, 1995; Galgiani, 2000)

Pneumonia, chronic progressive, fibrocavitary: 200-400 mg daily for 12 months (Catanzaro, 1995; Galgiani, 2000)

Pneumonia, diffuse: Consolidation after amphotericin B induction: 400 mg daily for 12 months (lifelong in chronically immunosuppressed) (Galgiani, 2005)

Coccidioidomycosis, prophylaxis: Oral:

HIV-infected, positive serology, CD4+ count <250 cells/microL (unlabeled use): 400 mg once daily (CDC, 2009)

Solid organ transplant (unlabeled use): **Note:** Prophylaxis regimens in this setting have not been established; the following regimen has been proposed for transplant recipients who maintain residence in a *Coccidioides* spp endemic area.

Previous history >12 months prior to transplant: 200 mg once daily for 6-12 months (Vikram, 2009; Vucicevic, 2011)

Previous history ≤12 months prior to transplant: 400 mg once daily, lifelong treatment (Vikram, 2009; Vucicevic, 2011)

Positive serology before or at transplant: 400 mg once daily, lifelong treatment; if serology is negative at 12 months, consider a dose reduction to 200 mg daily (Vikram, 2009; Vucicevic, 2011)

No history (at risk for *de novo* post-transplant disease): some clinicians treat with 200 mg daily for 6-12 months (Vucicevic, 2011)

Cryptococcosis: Oral, I.V.:

Meningitis: Manufacturer's recommendation: 400 mg for 1 dose, then 200-400 mg once daily for 10-12 weeks following negative CSF culture

HIV-infected:

Meningitis (in patients amphotericin B resistant or intolerant): Induction: 400-800 mg once daily for 4-6 weeks with concomitant flucytosine (CDC, 2009) **or**800-1200 mg once daily with concomitant flucytosine for 6 weeks (Perfect, 2010)

Consolidation: 400 mg once daily for 8 weeks (CDC, 2009)

Maintenance (suppression): 200 mg once daily lifelong or until CD4+ count >200 (CDC, 2009)

Pulmonary (immunocompetent) (unlabeled use): 400 mg once daily for 6-12 months (Perfect, 2010)

Dosing: Renal Impairment

No adjustment for vaginal candidiasis single-dose therapy.

For multiple dosing in adults, administer loading dose of 50-400 mg, then adjust daily doses as follows (dosage reduction in children should parallel adult recommendations): Cl_{cr} ≤50 mL/minute (no dialysis): Administer 50% of recommended dose daily

Intermittent hemodialysis (IHD): Dialyzable (50%): May administer 100% of daily dose (according to indication) after each dialysis session. Alternatively, doses of 200-400 mg every 48-72 hours **or** 100- 200 mg every 24 hours have been recommended. **Note:** Dosing dependent on the assumption of 3 times/week, complete IHD sessions (Heintz, 2009).

Continuous renal replacement therapy (CRRT) (Heintz, 2009; Trotman, 2005): Drug clearance is highly dependent on the method of renal replacement, filter type, and flow rate. Appropriate dosing requires close monitoring of pharmacologic response, signs of adverse reactions due to drug accumulation, as well as drug concentrations in relation to target trough (if appropriate). The following are general recommendations only (based on dialysate flow/ultrafiltration rates of 1-2 L/hour and minimal residual renal function) and should not supersede clinical judgment:

CVVH: Loading dose of 400-800 mg followed by 200-400 mg every 24 hours

CVVHD/CVVHDF: Loading dose of 400-800 mg followed by 400-800 mg every 24 hours (CVVHD or CVVHDF) **or** 800 mg every 24 hours (CVVHDF)

Note: Higher maintenance doses of 400 mg every 24 hours (CVVH), 800 mg every 24 hours (CVVHD), and 500-600 mg every 12 hours (CVVHDF) may be considered when treating resistant organisms and/or when employing combined ultrafiltration and dialysis flow rates of ≥2 L/hour for CVVHD/CVVHDF (Heintz, 2009; Trotman, 2005)

Common side effect**:** Headache , dizziness ,Nausea ,abdominal pain , vomiting ,

hypokalemia.

Pregnancy Risk Factor**:** C (single dose for vaginal candidiasis)/D (all other indications).