Itraconazole:

Class: Antifungal Agent.

Indications:

Oral capsules: Treatment of susceptible fungal infections in immunocompromised and immunocompetent patients including blastomycosis and histoplasmosis; indicated for aspergillosis (in patients intolerant/refractory to amphotericin B), and onychomycosis of the toenail and fingernail (in nonimmunocompromised patients)

Oral solution: Treatment of oral and esophageal candidiasis

Available dosage form in the hospital: 100MG CAP

Trade Names:

Dosage:

Note: Doses >200 mg daily should be administered in 2 divided doses.

-Aspergillosis: Oral: 200-400 mg daily. **Note:** For life-threatening infections, administer a loading dose of 200 mg 3 times daily (total: 600 mg daily) for the first 3 days of therapy. Continue treatment for at least 3 months and until clinical and laboratory evidence suggest that infection has resolved.

-Aspergillosis, invasive (salvage therapy): Duration of therapy should be a minimum of 6-12 weeks or throughout period of immunosuppression: Oral: 200-400 mg daily;**Note:** 2008 IDSA guidelines recommend 600 mg/day for 3 days, followed by 400 mg daily (Walsh, 2008).

-*Appropriate use:* Itraconazole should **NOT** be used for voriconazole-refractory aspergillosis since the same antifungal and/or resistance mechanism(s) may be shared by both agents. Itraconazole oral solution and capsule formulations are not bioequivalent or interchangeable. Due to variable bioavailability of oral preparations, therapeutic drug monitoring is advisable (Walsh, 2008).

-Aspergillosis, allergic (ABPA, sinusitis): Oral: 200 mg/day; may be used in conjunction with corticosteroids (Walsh, 2008)

-Blastomycosis: Oral: Initial: 200 mg once daily; if no clinical improvement or evidence of progressive infection, may increase dose in increments of 100 mg up to maximum of 400 mg daily. **Note:** For life-threatening infections, administer a loading dose of 200 mg 3 times daily (total: 600 mg daily) for the first 3 days of therapy. Continue treatment for at least 3 months and until clinical and laboratory evidence suggest that infection has resolved.

-*Alternative dosing (Chapman, 2008):* 200 mg 3 times daily for 3 days, then 200 mg twice daily for 6-12 months; in moderately-severe to severe infection, therapy should be initiated with ~2 weeks of amphotericin B.

-Candidiasis: Oral:

-*Esophageal:*

-Oral solution: 100-200 mg once daily for a minimum of 3 weeks; continue dosing for 2 weeks after resolution of symptoms

-Oral capsules: Canadian labeling (not in U.S. labeling): 100 mg once daily for 4 weeks; increase dose to 200 mg once daily in patients with AIDS and neutropenic patients

-*Oropharyngeal:*

-Oral solution: 200 mg once daily for 1-2 weeks; in patients unresponsive or refractory to fluconazole: 100 mg twice daily (clinical response expected in 2-4 weeks)

-Oral capsules: Canadian labeling (not in U.S. labeling): 100 mg once daily for 2 weeks; increase dose to 200 mg once daily in patients with AIDS and neutropenic patients

-Chromomycosis: Canadian labeling (not in U.S. labeling): Oral: 200 mg once daily for 6 months (when due to *Fonsecaea pedrosoi*) or 100 mg once daily for 3 months (when due to *Cladosporium carrioni*)

-Coccidioidomycosis (nonprogressive, nondisseminated disease): 200 mg twice daily or 3 times/day (Galgiani, 2005)

-Histoplasmosis: Oral: Manufacturer labeling: Initial: 200 mg once daily; if no clinical improvement or evidence of progressive infection, may increase dose in increments of 100 mg up to maximum of 400 mg daily. **Note:** For life-threatening infections, administer a loading dose of 200 mg 3 times daily (total: 600 mg daily) for the first 3 days of therapy. Continue treatment for at least 3 months and until clinical and laboratory evidence suggest that infection has resolved.

-*Alternative dosing (Wheat, 2007):* 200 mg 3 times daily for 3 days, then 200 mg twice daily (or once daily in mild-moderate disease) for 6-12 weeks in mild-moderate disease or ≥12 months in progressive disseminated or chronic cavitary pulmonary histoplasmosis; in moderately-severe to severe infection, therapy should be initiated with ~2 weeks of a lipid formation of amphotericin B.

-*Long-term suppression therapy:* 200 mg/day (CDC, 2009b)

-Meningitis: Oral:

-*Coccidioides:* 400-600 mg/day (Galgiani, 2005)

-*Coccidioides, HIV-positive (unlabeled use):* 200 mg 3 times/day for 3 days, then 200 mg twice daily; maintenance: 200 mg twice daily life-long (CDC, 2009b)

-*Appropriate use:* Fluconazole is preferred for meningeal infections (CDC, 2009b; Galgiani, 2005).

-Onychomycosis: Oral: 200 mg once daily for 12 consecutive weeks; alternative "pulse-dosing" may be considering for fingernail involvement only: 200 mg twice daily for 1 week; repeat 1-week course after 3-week off-time

-Onychomycosis (toenails with or without fingernail involvement): Canadian labeling (not in U.S. labeling): Oral: "Pulse-dosing": 200 mg twice daily for 1 week; repeat 1-week course twice with 3-week off-time between each course

-Paracoccidioidomycosis: Canadian labeling (not in U.S. labeling): Oral: 100 mg once daily for 6 months

-Penicilliosis, HIV-positive (unlabeled use): Oral: 400 mg daily for 8 weeks (mild disease) or 10 weeks (severe infections). In severely-ill patients, initiate therapy with 2 weeks of amphotericin B. Maintenance: 200 mg daily (CDC, 2009b)

-Pityriasis versicolor: Canadian labeling (not in U.S. labeling): Oral: 200 mg once daily for 7 days

-Pneumonia: Oral:

-*Coccidioides:* Mild-to-moderate: 200 mg twice daily

-*Coccidioides, HIV-positive (focal pneumonia):* 200 mg 3 times/day for 3 days, then 200 mg twice daily (CDC, 2009b)

- Sporotrichosis: Oral:

-*Lymphocutaneous:* 100-200 mg/day for 3-6 months (Kauffman, 2007)

-Canadian labeling (not in U.S. labeling): 100 mg once daily for 3 months

-*Osteoarticular and pulmonary:* 200 mg twice daily for ≥1 years (may use amphotericin B initially for stabilization) (Kauffman, 2007)

-Tinea corporis or tinea cruris: Canadian labeling (not in U.S. labeling): Oral: 100 mg once daily for 14 consecutive days or 200 mg once daily for 7 consecutive days.**Note:** Equivalency between regimens not established.

-Tinea pedis: Canadian labeling (not in U.S. labeling): Oral: 100 mg once daily for 28 consecutive days or 200 mg twice daily for 7 consecutive days. **Note:** Equivalency between regimens not established. Patients with chronic resistant infection may benefit from lower dose and extended treatment time (100 mg once daily for 28 days)

Renal Impairment :

The manufacturer's labeling states to use with caution in patients with renal impairment. Limited data suggests that no dosage adjustments are required in renal impairment; wide variations observed in plasma concentrations versus time profiles in patients with uremia, or receiving hemodialysis or continuous ambulatory peritoneal dialysis (Boelaert, 1988).

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Arnoff,2007:

CLcr>10 ml/min :no adjustment recommended

CLcr <10ml/min : administer 50% of normal dose .

Poorly dialyzable ;no supplemental dose or dosage adjustment necessary ,including patients on intermittent hemodialysis ,peritoneal dialysis , or continuous renal replacement therapy (eg CVVHD).

Hepatic impairment : No dosage adjustment provided in manufacturer's labeling; however, use caution and monitor closely for signs/symptoms of toxicity.

Common side effect:

Gastrointestinal: Nausea , diarrhea.

Cardiovascular: Edema , hypertension , chest pain .

Central nervous system: Headache , fever , dizziness .

Dermatologic: Rash , pruritus .

Endocrine & metabolic: Hypertriglyceridemia , hypokalemia .

Pregnancy Risk Factor: C