Itraconazole

Antifungal Class:
Azoles

Antifungal Spectrum:
Opportunisitic yeasts: *Candida albicans*, *Candida tropcialis*, *Cryptococcus neoformans*, *Candida glabrata* (variable activity), *Candida krusei* (variable activity)
Opportunistic hyaline moulds: *Aspergillus spp*., *Scedosporium spp*. (variable activity)
Dimorphic moulds: *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, *Parracoccidioides brasiliensis*, *Sporothrix schenkii*, *Penicillium marneffei*
Zygomycetes: *Entomophthorales* (variable activity)
Dematiaceous moulds: variable activity

Mechanism of Action:
Inhibits fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis and inhibits cell membrane formation.

Pharmacodynamics:
AUC:MIC of the pathogen strongly correlates with efficacy in Candida species. This may vary in differing species.

Pharmacokinetics:
Tmax: 1.5-4 hours; Cmax:10 mcg/ml; Vd: 10.7 L/Kg; Total Clearance: 3.8 ml/min/Kg; Table 2

Adverse Effects:
Gastrointestinal: nausea, vomiting, abdominal pain
Cardiovascular System: edema, hypertension
Dermatologic: skin rashes, pruritus
Central Nervous System: headache, dizziness, fatigue
Endocrine & metabolic: hypertrigliceridemia, decreased libido, hypokalemia
Hepatic: abnormal LFTs, hepatitis
Renal: albuminuria

Dosage:
Capsule: 100 mg
Injection, solution: 10 mg/mL (25 mL)
Solution, oral: 100mg/10mL (150 mL)

Adults:
Oral: 100-400 mg/day (capsules); 2.5 mg/kg (HP-beta-CD solution)
Life-threatening infections - loading dose: 600 to 800 mg/day for 3-5 days
maintenance dose: 400 to 600 mg/day
Intravenous: 200 mg twice a day for 2 days, followed by 200 mg once daily for a maximum of 14 days altogether

Children < 18 years:
Oral: 5 to 8 mg/kg/d with a loading dose of 4 mg/kg three times a day for the first three days (capsules); 2.5 mg/kg twice a day (HP-beta-CD solution)

Disease state based dosing:
Renal failure: Oral itraconazole does not need adjusted; intravenous itraconazole is contraindicated in patients with a creatinine clearance less than 30 mL/min.

Hepatic failure: The elimination half-life can be prolonged, and additional hepatic toxicity or possible drug interactions should be carefully monitored.

Contraindications/Warnings/Precautions:
Contraindications: Concurrent administration with astemizole, cisapride, dofetilide, ergot derivatives, lovastatin, midazolam, pimozide, quinide, simvastatin

Precautions: Rare cases of serious cardiovascular events, including death, ventricular tachycardia, and torsades with concominant cisapride administration.

Drug Interactions:
Table 4.
Itraconazole is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering itraconazole with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.

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

Monitoring Requirements:
Plasma levels: 0.5 mcg/mL at trough for invasive fungal infections

Brand names/Manufacturer: