Voriconazole

Antifungal Class:
Azoles (Specifically triazoles

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

Mechanism of Action:
Inhibits fungal cytochrome P450 3A dependent enzyme, decreases ergosterol synthesis (prinicipal sterol in fungal cell wall membrane) and inhibits cell membrane formation.

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

Pharmacokinetics:
Tmax: 1-2hours
Cmax:1.5-2.3 mcg/ml
Vd: 2-4 L/Kg
Protein binding: 58%
Table 2

Adverse Reaction:
Ocular: visual changes (photophobia, color changes, increased or decreased visual acuity, or blurred vision)
Cardiovascular System: tachycardia, hypertension, hypotension, vasodilation, peripheral edema
Central Nervous System: fever, chills, headache, hallucinations, dizziness
Endocrine: hypokalemia, hypomagnesemia
Gastrointestinal: nausea, vomiting, abdominal pain, diarrhea, xerostomia
Hematologic: thrombocytopenia
Hepatic: alkaline phosphatase increased, serum transaminases increased
Renal: acute renal failure

Dosage:
Injection, powder for reconstitution: 200 mg
Tablet: 50 mg, 200 mg

Adults and pediatric patients > 2 years
IV: 6 mg/kg BID on day 1, followed by 4 mg/kg BID
PO: 400 mg BID on day 1 (<40 kg: 200 mg BID), followed by 200 mg BID (<40 mg: 100 mg q12h)

Disease state based dosing:
Renal failure: No dosage adjustment necessary. Patients with CrCl < 50 ml/min should receive voriconazole by the oral route.
Hepatic failure: In patients with mild to moderate hepatic function abnormalities (Child-Pugh category A and B), half of the daily maintenance dosage is recommended after the initial loading dose. Recommendations for severe liver failure (Child-Pugh category C) are lacking.

Dosing during Continuous Renal Replacement Therapy
CVVH (Continuous venovenous hemofiltration): 1-2g IV q12h
CVVHD (Continuous venovenous hemodialysis): 2g IV q12h
CVVHDF (Continuous venovenous hemodiafiltration) 2g IV q12h
Note: CVVH is mainly for fluid removal alone. Many institutions will employ more CVVHD or CVVHDF which combine dialysis with fluid removal.
Note: The oral bioavailability of voriconazole is estimated to be 96%. Consider 2 loading doses of 6mg/kg PO q12h

Contraindications/Warnings/Precautions:
Contraindications: Coadministration of CYP3A4 substrates which may lead to QT prolongation (cisapride, pimozide, quinidine); coadministration with long acting barbiturates, carbamazepine, ergot alkaloids, rifampin, rifabutin, and sirolimus

Precautions: Visual changes are commonly associated with treatment. Serious hepatic reactions have occurred during treatment, primarily in patients with serious concominant medical conditions.

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

Pregnancy Risk Factor:
D

Monitoring parameters:
Hepatic, renal, visual function.

Brand names/Manufacturer:

- VFEND (Pfizer - UNITED KINGDOM, USA, PORTUGAL, IRELAND, FRANCE, SPAIN, AUSTRALIA, HUNGARY, SWEDEN, DENMARK, ISRAEL, FINLAND, BELGIUM, NORWAY, ITALY, GERMANY, HONG KONG)