Voriconazole

Note: Voriconazole does not cover zygomycoses (Mucor, Rhizopus, Cunninghamella, etc)

Acceptable uses (ID consult advised):
- **Aspergillosis** (please refer to prior definitions)
- Oncologic neutropenic and BMT populations:
  - **Definite** (biopsy-proven) invasive non-zygomycete filamentous fungal infections
  - **Probable** invasive non-zygomycete filamentous fungal infections
  - Empiric therapy in patients with **possible** aspergillosis (follow-up diagnostic studies are highly recommended)
- Other patient populations:
  - Definite infections or as otherwise deemed appropriate after consultation with the Infectious Diseases service or the ASP
  - *Pseudallescheria boydii (Scedosporium spp), Fusarium spp.* Voriconazole is recommended as first-line therapy
  - Alternative therapy for *C. krusei* if susceptible and oral therapy is desired in stable patient.

Unacceptable uses:
- **Candidiasis / Neutropenic fever**: Voriconazole should not be used as first-line therapy for the treatment of candidiasis or for empiric therapy in patients with neutropenic fever.
- Treatment of positive urine cultures due to resistant *Candida* spp.

Dose
- Loading dose: 6 mg/kg IV/PO q12h x 2 doses
- Maintenance dose: 4 mg/kg IV/PO q12h
- Patients receiving concomitant phenytoin or efavirenz should receive following maintenance doses of voriconazole due to induced hepatic clearance by phenytoin and efavirenz.
  - Intravenous: 5 mg/kg q12h
  - Oral: 400 mg q12h (wt >40 kg) or 200 mg Q12h (wt <40kg)
  - Efavirenz dose should be decreased to 300 mg PO daily
  - Monitor phenytoin levels and adverse events
  - Dose escalation may be necessary for some patients due to subtherapeutic levels
- Voriconazole IV is packaged with a cyclodextrin vehicle which can accumulate in patients with renal dysfunction. The clinical significance of risk vs benefit of using IV voriconazole in patients with renal dysfunction is unknown.

Therapeutic monitoring
- Obtaining voriconazole trough levels should be considered in patients who are:
  - not responding to therapy after at least 5 days of therapy using a mg/kg dosing strategy
  - receiving concomitant drugs that may increase or decrease voriconazole levels
experiencing adverse events due to voriconazole
- experiencing GI dysfunction
- Voriconazole trough levels should be obtained 5-7 days after start of therapy
- Goal trough: 1-5.5 mcg/mL. Levels < 1 mcg/mL have been associated with clinical failures and levels >5.5 mcg mL with toxicity

Drug interactions
- Voriconazole is an inhibitor and is metabolized by cytochrome P450; therefore co-administration with other agents that are cytochrome P450 substrates, inducers, or inhibitors will result in significant drug interactions.
- **You must check for potential drug interactions when initiating voriconazole therapy or starting a new medication in patients already receiving voriconazole therapy.**
- Administration of the following agents with voriconazole is contraindicated:
  - Sirolimus, Rifampin, Rifabutin, Carbamazepine, Terfenadine, Astemizole, Cisapride, Pimozide, Quinidine, long-acting barbiturates, Ritonavir (400 mg BID), St. John’s Wort, and ergot alkaloids
- Voriconazole inhibits metabolism of the following agents: dose reductions and close monitoring are recommended when voriconazole is used with agents concomitantly:
  - Tacrolimus - reduce tacrolimus dose to ⅓ and monitor levels
  - Cyclosporine - reduce cyclosporine dose to ½ and monitor drug levels
  - Omeprazole - reduce omeprazole dose to ½
  - Warfarin - monitor INR
  - Ritonavir low dose (100 mg q12h) - avoid this combination unless benefit outweighs risk
  - Sulfonylureas, statins (avoid Lovastatin and Simvastatin), vinca alkaloids, calcium channel blockers, benzodiazepines (avoid midazolam and triazolam), oral contraceptives, Alfentanil, and Methadone – monitor effect of the drugs and consider decreasing dose when Voriconazole is added.

Toxicity
- Visual disturbances (~30%) usually self-limited, rash, fever, elevations in hepatic enzymes.
- Monitoring: hepatic panel at baseline and every 1-2 weeks after.