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 studied 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 (Scedosporim 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 m/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.