

# Posaconazole

Posaconazole is a broad spectrum azole anti-fungal agent. It has *in vitro* activity against Candida, Aspergillus, Zygomycosis and Fusarium spp.

## Acceptable uses

- Treatment of invasive zygomycosis in combination with Amphotericin B
- Monotherapy for zygomycosis after 7 days of combination therapy with Amphotericin B
- **Note: posaconazole requires up to 7 days to achieve steady state concentrations. ID consult is advised.**

## Unacceptable uses

- Candidiasis/neutropenic fever
- Primary treatment of aspergillosis

## Dose

**Note: each dose should be given with a full meal or with liquid nutritional supplements if patients cannot tolerate full meals.**

- Loading dose: 200 mg PO q6h for 7 days
- Maintenance dose: 400 mg PO q8-12h

## Drug Interactions

- Posaconazole is an inhibitor and is metabolized by cytochrome P4503A4; 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 Posaconazole therapy or starting a new medication in patients already receiving Posaconazole therapy.**
- Administration of the following agents with Posaconazole is contraindicated:
  - Terfenadine, Astemizole, Pimozide, Cisapride, Quinidine, Sirolimus, Halofantrine and ergot alkaloids
- Posaconazole inhibits metabolism of the following agents. Dose reductions and close monitoring are recommended when Posaconazole is used with agents concomitantly:
  - Tacrolimus – reduce Tacrolimus dose to  $\frac{1}{3}$  and monitor levels
  - Cyclosporine – reduce Cyclosporine dose to  $\frac{3}{4}$  and monitor drug level
  - Midazolam – consider dose reducing
  - Cimetidine, Rifabutin, Efavirenz and Phenytoin – unless the benefit outweighs the risk, AVOID concomitant use. If used together, monitor effect of the drugs and consider decreasing dose when Posaconazole is added
  - Statins (avoid Lovastatin and Simvastatin), vinca alkaloids, calcium channel blockers, Digoxin, Atazanavir, Ritanovir, QTc prolonging drugs (e.g. Amiodarone and Erythromycin) – monitor effect of the drugs and consider decreasing dose when Posaconazole is added
  - Cimetidine, Rifabutin, Phenytoin, Efavirenz, Esomeprazole, Metoclopramide may decrease Posaconazole blood levels.

## Toxicity

- GI upset (~40%), headaches, elevation in hepatic enzymes. Rare but serious effects include QTc prolongation
- Monitoring: Hepatic enzymes at baseline and every 1-2 weeks after