Voriconazole:

Class: Antifungal.

Indications:

Treatment of invasive aspergillosis; treatment of esophageal candidiasis; treatment of candidemia (in non-neutropenic patients); treatment of disseminated *Candida*infections of the skin and viscera; treatment of serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* spp (including *Fusarium solani*) in patients intolerant of, or refractory to, other therapy

Available dosage form in the hospital : 200MG FILM-COATED TABLETS, 200MG VIAL.

Dosage:

-**Aspergillosis, invasive, including disseminated and extrapulmonary infection:** Duration of therapy should be a minimum of 6-12 weeks or throughout period of immunosuppression (Walsh, 2008):

-I.V.: Initial: Loading dose: 6 mg/kg every 12 hours for 2 doses; followed by maintenance dose of 4 mg/kg every 12 hours

-Oral: Maintenance dose:

-Manufacturer's recommendations:

-Patients <40 kg: 100 mg every 12 hours; maximum: 300 mg/day

-Patients ≥40 kg: 200 mg every 12 hours; maximum: 600 mg/day

-IDSA recommendations (Walsh, 2008): May consider oral therapy in place of I.V. with dosing of 4 mg/kg (rounded up to convenient tablet dosage form) every 12 hours; however, I.V. administration is preferred in serious infections since comparative efficacy with the oral formulation has not been established.

-**Scedosporiosis, fusariosis:**

-I.V.: Initial: Loading dose: 6 mg/kg every 12 hours for 2 doses; followed by maintenance dose of 4 mg/kg every 12 hours

-Oral: Maintenance dose:

-Patients <40 kg: 100 mg every 12 hours; maximum 300 mg/day

-Patients ≥40 kg: 200 mg every 12 hours; maximum: 600 mg/day

-**Candidemia and other deep tissue *Candida* infections:** Treatment should continue for a minimum of 14 days following resolution of symptoms or following last positive culture, whichever is longer.

-I.V.: Initial: Loading dose 6 mg/kg every 12 hours for 2 doses; followed by maintenance dose of 3-4 mg/kg every 12 hours

-Oral:

-Manufacturer's recommendations: Maintenance dose:

-Patients <40 kg: 100 mg every 12 hours; maximum: 300 mg/day

-Patients ≥40 kg: 200 mg every 12 hours; maximum: 600 mg/day

-IDSA recommendations (Pappas, 2009): Initial: Loading dose: 400 mg every 12 hours for 2 doses; followed by 200 mg every 12 hours

-Endophthalmitis, fungal (unlabeled use; Pappas, 2009): I.V.: 6 mg/kg every 12 hours for 2 doses, then 3-4 mg/kg every 12 hours

-Esophageal candidiasis: Oral: Treatment should continue for a minimum of 14 days, and for at least 7 days following resolution of symptoms:

-Patients <40 kg: 100 mg every 12 hours; maximum: 300 mg/day

-Patients ≥40 kg: 200 mg every 12 hours; maximum: 600 mg/day

-Meningitis (secondary to contaminated [eg, *Exserohilum rostratum*] steroid products) (unlabeled use) (CDC [parameningeal], 2012; Kauffman, 2013): Note:Consult an infectious disease specialist and current CDC guidelines for specific treatment recommendations. Therapy duration is ≥3 months; trough serum concentrations must be maintained between 2-5 mcg/mL.

-I.V.: 6 mg/kg every 12 hours. If patient does not improve or has severe disease, consider adding amphotericin B (liposomal)

-Oral (only in mild disease in adherent patients whose trough concentrations/response to therapy can be closely monitored): 6 mg/kg every 12 hours (CDC [parameningeal], 2012)

-Osteoarticular infection involving the spine, discitis, epidural abscess or vertebral osteomyelitis (secondary to contaminated [eg, *Exserohilum rostratum*] steroid products) (unlabeled use) (CDC [osteoarticular], 2012; Kauffmann, 2013): I.V.: 6 mg/kg every 12 hours for ≥3 months. **Note:** Consult an infectious disease specialist and current CDC guidelines for specific treatment recommendations. Trough serum concentrations must be maintained between 2-5 mcg/mL. If patient has severe disease, consider adding amphotericin B (liposomal). Patients may be switched to oral therapy if condition has improved or stabilized.

-Osteoarticular infection not involving the spine (secondary to contaminated [eg, *Exserohilum rostratum*] steroid products) (unlabeled use) (CDC [osteoarticular], 2012; Kauffman, 2013): Note: Consult an infectious disease specialist and current CDC guidelines for specific treatment recommendations. Therapy duration is ≥3 months. Trough serum concentrations must be maintained between 2-5 mcg/mL.

-I.V.: 6 mg/kg every 12 hours for 2 doses, then 4 mg/kg every 12 hours. If patient has severe disease, consider adding amphotericin B (liposomal)

-Oral (only in mild disease in adherent patients whose trough concentrations/response to therapy can be closely monitored): 6 mg/kg every 12 hours for 2 doses, then 4 mg/kg every 12 hours

Dosage adjustment in patients unable to tolerate treatment:

-I.V.: Dose may be reduced to 3-4 mg/kg every 12 hours, depending upon condition

-Oral: Dose may be reduced in 50 mg decrements to a minimum dosage of 200 mg every 12 hours in patients weighing ≥40 kg (100 mg every 12 hours in patients <40 kg).

Dosage adjustment in patients receiving concomitant CYP450 enzyme inducers or substrates:

-Efavirenz: Oral: Increase maintenance dose of voriconazole to 400 mg every 12 hours and reduce efavirenz dose to 300 mg once daily; upon discontinuation of voriconazole, return to the initial dose of efavirenz

-Phenytoin:

-I.V.: Increase voriconazole maintenance dosage to 5 mg/kg every 12 hours

-Oral: Increase voriconazole dose to 400 mg every 12 hours in patients ≥40 kg (200 mg every 12 hours in patients <40 kg)

Renal Impairment:

-In patients with Cl_{cr} <50 mL/minute, accumulation of the intravenous vehicle (cyclodextrin) occurs. After initial I.V. loading dose, oral voriconazole should be administered to these patients, unless an assessment of the benefit:risk to the patient justifies the use of I.V. voriconazole. Monitor serum creatinine and change to oral voriconazole therapy when possible.

-Oral: Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on intermittent hemodialysis, peritoneal dialysis, or continuous renal replacement therapy (eg, CVVHD).

Note: I.V. dosing **NOT** recommended since cyclodextrin vehicle is cleared at half the rate of voriconazole and may accumulate.

Hepatic Impairment:

-Mild-to-moderate hepatic dysfunction (Child-Pugh class A or B): Following standard loading dose, reduce maintenance dosage by 50%

-Severe hepatic impairment: Should only be used if benefit outweighs risk; monitor closely for toxicity

Common side effect:

Central nervous system: Hallucination (2% to 12%; auditory and/or visual and likely serum concentration-dependent), headache.

Ophthalmic: Visual disturbance

Renal: Increased serum creatinine .

Cardiovascular: Tachycardia

Dermatologic: Skin rash .

Endocrine & metabolic: Hypokalemia .

Pregnancy Risk Factor: D