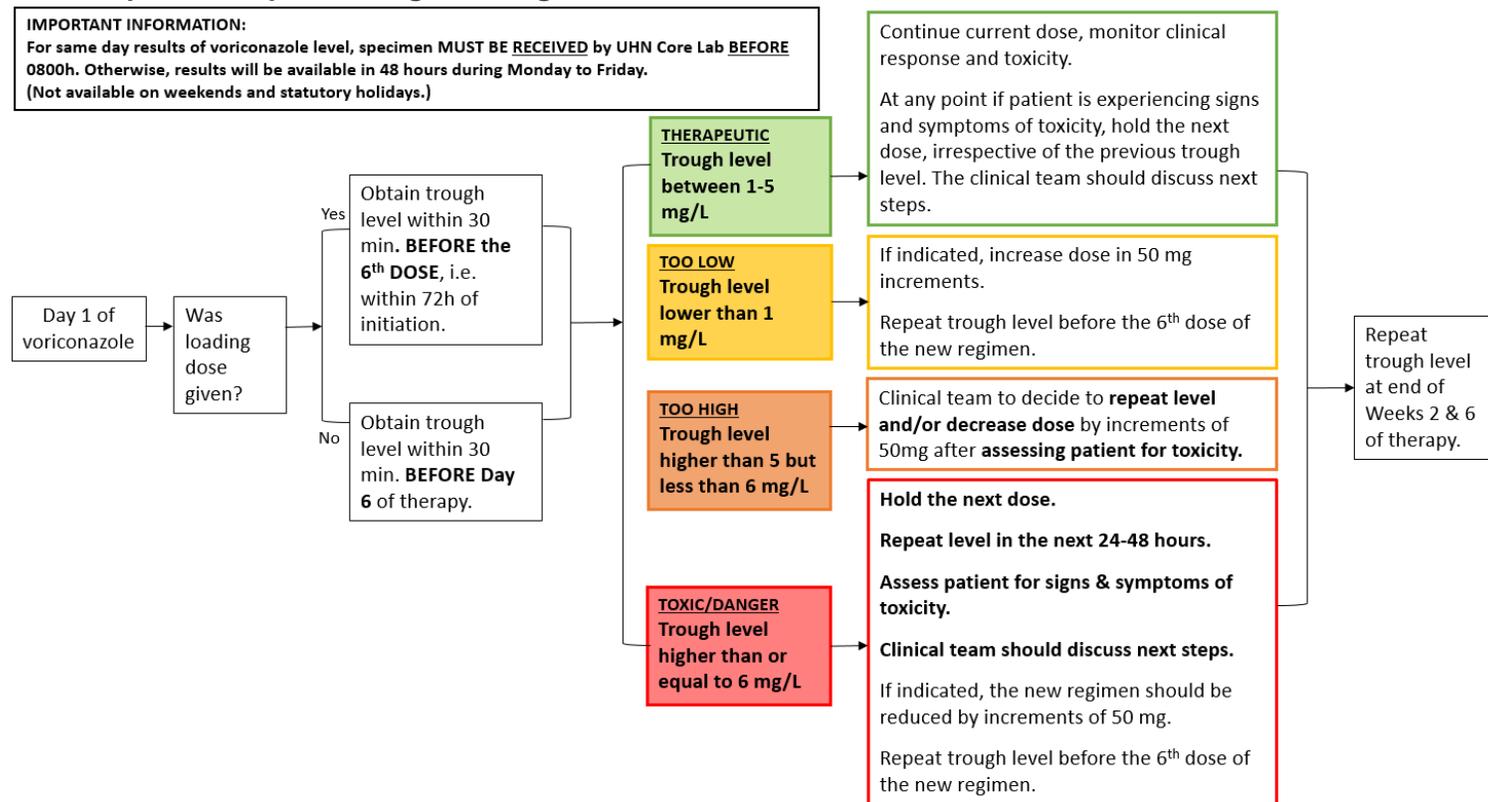


✦ For guidance on antifungal selection, see Empiric Use of Antifungals

✦ Dose:

- Invasive aspergillosis: 6 mg/kg IV or PO Q12H x 2 doses, followed by 4 mg/kg IV or PO Q12H
- Invasive candidiasis (not 1st line): 6 mg/kg IV or PO Q12H x 2 doses, followed by 3 mg/kg IV or PO Q12H

✦ Accepted therapeutic range: 1-5 mg/L



✦ Rationale for monitoring voriconazole levels: safety and efficacy

- Associated with high level, neurotoxicity can present as visual and/or auditory hallucinations, altered mental status, agitation and involuntary myotonic movements.
 - IMPORTANT: neurotoxicity is to be *distinguished from transient visual disturbances* (photopsia), which can occur a few minutes after receiving voriconazole (PO or IV), and is related to higher doses, e.g. at loading dose. They generally resolve as therapy continues, therefore, it is not an indication to stop therapy.
- Transaminitis can be associated with trough level greater than 5.5-6 mg/L, with the potential development of hepatitis.
- Voriconazole is metabolized by CYP isoenzymes 2C9, 2C19, and 3A4. Drug-drug interactions involving voriconazole are common and wide-ranging. Examples (not exhaustive): cyclosporine, tacrolimus, tyrosine kinase inhibitors, sulfonylureas (glyburide, glicazide, glimepiride, glipizide), rifamycins, benzodiazepines, phenytoin, carbamazepine. Conduct a thorough review of potential interactions when initiating therapy and monitor drug levels accordingly if voriconazole is indicated. Addition of a medication that interacts with voriconazole should trigger a recheck of voriconazole level.
- Voriconazole has a non-linear relationship between dose and serum level, coupled with genetic polymorphism of 2C19, there is wide variability in serum level.
- Subtherapeutic level may be associated with poor clinical response to therapy.

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