Antifungal Drugs Monitoring

Indications for Ordering

- Optimize drug therapy and monitor patient adherence
- Predose (trough) concentration at steady state should be assessed

Test Description

Quantitative high-performance liquid chromatography-tandem mass spectrometry

Tests to Consider

Antifungal therapeutic monitoring

- Fluconazole, Quantitative by LC-MS/MS 0097621
- Itraconazole, Quantitative by LC-MS/MS 0098519
- Posaconazole, Quantitative by LC-MS/MS 2001739
- Voriconazole, Quantitation by LC-MS/MS 2001737

Disease Overview

Clinical issues

- Fluconazole is used in the prophylaxis and treatment of
  - *Candida* spp
  - *Cryptococcus neoformans*
  - *Blastomycosis dermatitidis*
  - *Coccidioides immitis*
- Itraconazole is used in the treatment of
  - *Blastomycosis dermatitidis*
  - *Histoplasmosis capsulatum*
  - *Aspergillus* spp
- Posaconazole is used in the prophylaxis and treatment of
  - *Candida* spp
  - *Aspergillus* spp
  - Dermatophytes
  - *Zygomycetes*
- Voriconazole is used in the treatment of
  - *Candida* spp
  - *Aspergillus* spp
  - *Fusarium* spp
  - *Scedosporium*
- Due to toxicity risk and need for optimal efficacy in patient therapy, all antifungal treatment should be monitored with trough levels

Physiology

Azole antifungal drugs inhibit synthesis of ergosterol

- Ergosterol is a major component of fungal cell membranes
- Inhibition of ergosterol causes increased permeability of cell membranes and cell death

Drug profile

Drug/drug interactions can occur with drugs that induce or inhibit metabolism of antifungal drugs, such as drugs that affect the CYP3A4 pathway

- Antifungals are contraindicated for patients taking drugs that are substrates for the CYP3A4 pathway
  - QT interval prolongation may occur, with torsade de pointes arrhythmias possible

Test Interpretation

Analytical sensitivity

- Voriconazole, posaconazole, itraconazole, and metabolites – limit of quantification is 0.1 µg/mL
- Fluconazole – limit of quantification is 1.0 µg/mL

Results

Drug	Therapeutic range (µg/mL)	Toxic level (µg/mL)
Fluconazole	5.0-20.0	Not well established
Itraconazole	Systemic – >1.0 Localized – >0.5	Not well established
Posaconazole	>0.7	Not well established
Voriconazole	1.0-5.5	>6.0

Limitations

Ketoconazole not detected