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
  o Candida spp
  o Cryptococcus neoformans
  o Blastomyces dermatitidis
  o Coccidioides immitis
- Itraconazole is used in the treatment of
  o Blastomyces dermatitidis
  o Histoplasmosis capsulatum
  o Aspergillus spp
- Posaconazole is used in the prophylaxis and treatment of
  o Candida spp
  o Aspergillus spp
  o Dermatophytes
  o Zygomycetes
- Voriconazole is used in the treatment of
  o Candida spp
  o Aspergillus spp
  o Fusarium spp
  o 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
  o 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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Therapeutic range (μg/mL)</th>
<th>Toxic level (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>5.0-20.0</td>
<td>Not well established</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Systemic – &gt;1.0</td>
<td>Not well established</td>
</tr>
<tr>
<td></td>
<td>Localized – &gt;0.5</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>&gt;0.7</td>
<td>Not well established</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>1.0-5.5</td>
<td>&gt;6.0</td>
</tr>
</tbody>
</table>

Limitations
Ketoconazole not detected