CANDIDA INFECTIONS - TREATMENT GUIDELINES IN ADULT PATIENTS (ABBREVIATED)

GUIDELINES:

These are the 2010 Guidelines for the Treatment of Candida species infections in adult patients. These recommendations take into account drugs available on the New York-Presbyterian Hospital Formulary, susceptibility of Candida sp. to antifungal agents, hospital specific Candida sp. susceptibilities, toxicities and drug interactions of the antifungals, and cost. A patient’s antifungal treatment history, history of positive fungal cultures, end-organ function, drug interaction potential, and level of immunosuppression corresponding to risk of non-Candida invasive fungal infections must always be taken into account. In addition, appropriate dosing for the patient’s weight, end-organ function, site of infection, and drug interactions are essential to improving outcomes and limiting the selection of more resistant Candida species. Historically, lower dosing of fluconazole (100-200 mg daily) for systemic infections has been associated with an increase in the development of azole-resistant Candida species, like C. glabrata.
Antifungal Therapy for the Treatment of Infections Caused by *Candida* species in Adult Patients

**Candidemia**
(Documented *Candida* species in blood)

**Invasive Candidiasis**
(positive *Candida* culture from sterile site and either fever >38.3°C or hypotension (SBP <90 mmHg or a decrease ≥30 mmHg) or signs of inflammation at a *Candida*-infected site)

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**Candiduria**
(Candida species identified in urine culture)

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Remove/change urinary bladder catheter if present and repeat urine micro/culture
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YES

NO

Persistently positive culture and symptomatic

Fluconazole 200 mg PO/IV q24h x 5 days

* Consider higher dose fluconazole or amphotericin B bladder irrigation x 3-5 days for persistent symptomatic candiduria

(voriconazole and micafungin are NOT expected to achieve adequate concentrations in the urine and should not be used to treat isolated candiduria)

1. Consider also treating candiduria in patients with neutropenia and patients who will undergo urologic manipulations

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**START EMPIRIC ANTIFUNGAL THERAPY**

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**Risk factors for fluconazole-resistant *Candida* sp.**
- History/colonization with *C. glabrata*, *C. krusei* or known fluconazole-resistant isolate
- Significant exposure to azole antifungals (e.g. > 2 weeks in the last 90 days)
- Hematologic malignancy
- HIV positive

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**YES**

Micafungin 100 mg IV q24h

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**NO**

**Hemodynamically unstable**

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**YES**

Hypotension (SBP <90, or ≥ 40 mmHg decrease from baseline in the absence of other causes) despite adequate fluid resuscitation or requiring vaso-active agents

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**NO**

Micafungin 100 mg IV q24h OR Lipid Amphotericin B 5 mg/kg IV q24h

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**Pre-emptive Antifungal Therapy**
(Early treatment of invasive candidiasis on the basis of an individual risk profile)

**Criteria:**
- Fever >38.3°C on broad spectrum antibiotics, AND
- *Candida* sp. colonization at ≥2 sites, AND
- At least TWO of the following risk factors: recent major abdominal surgery, currently receiving total parenteral nutrition (TPN), currently receiving renal replacement therapy, current central venous catheter (CVC), prolonged ICU stay

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**Candiduria**
(Candida species identified in urine culture)

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Remove/change urinary bladder catheter if present and repeat urine micro/culture
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Persistently positive culture and symptomatic

Fluconazole 200 mg PO/IV q24h x 5 days

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1. Consider also treating candiduria in patients with neutropenia and patients who will undergo urologic manipulations

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**Fluconazole 400 mg IV q24h (NYP/WGC)** OR **Fluconazole 800 mg IV q24h (NYP/C)**

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**Fluconazole 800 mg IV q24h**

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**LAST UPDATED 5/10/10**
Candida species identified
Without risk factors for fluconazole-resistance (see prior page)

**Species**
- **Candida albicans**
- **Candida parapsilosis**
- **Candida tropicalis**

**Candida glabrata**

**Candida krusei**

**Candida lusitanae**
OR other species

**PO Therapy**

**IV Therapy**

Fluconazole 400 mg (~6 mg/kg) IV q24h

Fluconazole 800 mg (~12 mg/kg) IV q24h OR
Voriconazole 6 mg/kg IV q12h x 2 doses, then 4 mg/kg IV q12h

Micafungin 100 mg IV q24h

Voriconazole 6 mg/kg PO q12h x 2 doses, then 4 mg/kg PO q12h
OR
Voriconazole 6 mg/kg PO q12h x 2 doses, then 4 mg/kg PO q12h (only if voriconazole MIC reported < 1 mcg/mL)

Fluconazole 800 mg (~12 mg/kg) PO q24h OR
Voriconazole 6 mg/kg PO q12h x 2 doses, then 4 mg/kg PO q12h (only if voriconazole MIC reported < 1 mcg/mL)

Voriconazole 6 mg/kg PO q12h x 2 doses, then 4 mg/kg IV q12h

ID Consult suggested

**Criteria for oral or via tube administration:**
- GI absorption likely normal
- Ability to receive oral dosage form (analogous to concomitant oral or via tube administration of any other meds)

**LAST UPDATED 5/10/10**
1. Antifungal agents comparisons

<table>
<thead>
<tr>
<th></th>
<th>Fluconazole</th>
<th>Itraconazole</th>
<th>Voriconazole</th>
<th>Posaconazole</th>
<th>Amphotericin B products</th>
<th>Micafungin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage forms</strong></td>
<td>IV/PO</td>
<td>PO</td>
<td>IV/PO</td>
<td>PO</td>
<td>IV</td>
<td>IV</td>
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<tr>
<td><strong>Oral bioavailability</strong></td>
<td>&gt;90%</td>
<td>55%</td>
<td>&gt;95%</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td><strong>Effect of gastric pH</strong></td>
<td>None</td>
<td>Decreased concentrations</td>
<td>None</td>
<td>? decreased with PPI</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>CSF penetration</strong></td>
<td>Excellent (~80%)</td>
<td>Poor (&lt;10%)</td>
<td>Good (40-60%)</td>
<td>N/A</td>
<td>N/A</td>
<td>Unknown, expected poor</td>
</tr>
<tr>
<td><strong>Elimination route</strong></td>
<td>Renal</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Unknown</td>
<td>Hepatic</td>
</tr>
<tr>
<td><strong>Renal dose adjustment</strong></td>
<td>Yes¹</td>
<td>No</td>
<td>No²</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Hepatic dose adjustment</strong></td>
<td>No</td>
<td>Yes³</td>
<td>Yes⁴</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Toxicities</strong></td>
<td>Hepatotoxicity (high doses and prolonged therapy)</td>
<td>GI Hepatotoxicity Negative inotropic effects</td>
<td>Visual disturbances Hepatotoxicity Rash Hallucinations</td>
<td>GI Hepatotoxicity</td>
<td>Nephrotoxicity Related reactions Electrolyte abnormalities</td>
<td>Phlebitis/thrombophlebitis Elevated transaminases Histamine release reaction</td>
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<tr>
<td><strong>Drug interaction potential</strong></td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>-</td>
<td>+</td>
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<tr>
<td><strong>Induction/inhibition</strong></td>
<td>Inhibits CYP3A4 and other CYP isoforms</td>
<td>Substrate and inhibitor of CYP3A4</td>
<td>Substrate and inhibitor CYP2C9&gt;CYP2C9&gt;CYP3A4</td>
<td>Inhibits 3A4</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

1 Fluconazole requires dose adjustment in renal dysfunction. For estimated CrCl <30mL/min or receiving hemodialysis or peritoneal dialysis, ½ the usual daily dose should be administered. For patients receiving continuous renal replacement therapy (CRRT), the usual dose should be administered.

2 Caution with use of IV formulation in patients with CrCl <50mL/min as cyclodextrin component accumulates (assessment of risk vs. benefit should be made)

3 Itraconazole has been associated with severe hepatotoxicity, including liver failure and death. Itraconazole use should be carefully monitored in patients with hepatic dysfunction.

4 Voriconazole requires dose adjustment in patients with hepatic dysfunction. For Child-Pugh Class A and B, reduce maintenance dose by ½ following usual loading dose. Use is not recommended in Child-Pugh Class C.

5 Micafungin pharmacokinetic data is unavailable for severe hepatic impairment