GUIDELINES FOR TREATMENT OF CANDIDEMIA IN ADULTS

General Statements:
- Yeast in a blood culture should **NOT** be considered a contaminant
- If there is a high suspicion that yeast growing in a blood culture is *Histoplasma* or *Cryptococcus*, do not use micafungin and consult Infectious Diseases
- Infectious Diseases consultation is strongly recommended in all cases of candidemia
- Blood cultures should be repeated every 24-48 hours until clearance has been documented
- Remove all intravascular catheters whenever possible. In neutropenic patients, as sources of candidiasis other than CVCs predominate, catheter removal should be considered on an individual basis
- Patients should have a dilated fundoscopic exam performed to rule out endophthalmitis within the first week after initiation of therapy
- Additional evaluation for metastatic foci (e.g. echocardiogram) should be considered in patients with persistently positive blood cultures
- Duration of therapy:
  - Patients with no evidence of metastatic complications should be treated for 14 days following the first negative blood culture
  - Patients with metastatic complications (e.g. endophthalmitis, endocarditis) should have an ID Consult to determine length of therapy
  - Neutropenic patients with no evidence of metastatic complications should be treated for 14 days following the first negative blood culture, provided neutropenia has resolved

### INITIAL THERAPY IN PATIENTS WITH POSITIVE BLOOD CULTURES

**Clinical Setting**
(Does Not Apply to Meningitis, Endocarditis, and Endophthalmitis)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Primary Therapy</th>
<th>Alternative Therapy</th>
</tr>
</thead>
</table>
| **Initial therapy for patients with yeast identified in blood culture (prior to species identification and susceptibilities)** | Micafungin 100 mg IV daily | Fluconazole 800 mg IV/PO daily⁷  
OR  
Liposomal Amphotericin B 3 mg/kg IV daily  
See comments 1 and 2 regarding use of fluconazole and Liposomal Amphotericin B |

### DEFINITIVE THERAPY IN PATIENTS WITH POSITIVE BLOOD CULTURES

**Clinical Setting**
(Does Not Apply to Meningitis, Endocarditis, and Endophthalmitis)

| Clinical Setting | Primary Therapy | Subsequent Therapy  
(once susceptibilities are available) |
|------------------|-----------------|---------------------|
| Candida albicans  
Candida dubliniensis  
Candida parapsilosis  
Candida tropicalis  
Candida lusitaniae | Micafungin 100 mg IV daily  
See comments 1 and 5 regarding primary use of fluconazole and voriconazole | Transition to fluconazole once patients are clinically stable, are no longer candidemic, and who have susceptible isolates  
Preferred:  
Fluconazole 800 mg x1 day, then 400 mg IV/PO daily⁷  
Alternatives:  
Voriconazole 6 mg/kg PO/IV q12h x2 doses, then 4 mg/kg PO/IV q12h⁸  
OR  
Liposomal Amphotericin B 3 mg/kg IV daily (C. lusitaniae is considered resistant to Amphotericin B) |
| Candida glabrata | Micafungin 100 mg IV daily  
See comments 1, 2, and 5 regarding primary use of fluconazole, voriconazole, and Liposomal Amphotericin B.  
Liposomal Amphotericin B is the preferred alternative primary therapy for infections due to C. glabrata | Transition to fluconazole or voriconazole in patients in whom an oral option is needed once they are clinically stable, are no longer candidemic, and have isolates in the following MIC ranges:  
Fluconazole: MIC ≤8  
Voriconazole: Only if fluconazole MIC >8 and voriconazole MIC is ≤0.5  
Preferred:  
Fluconazole 800 mg IV/PO daily⁷  
Alternatives:  
Voriconazole 6 mg/kg PO/IV q12h x2 doses, then 4 mg/kg PO/IV q12h⁸  
OR  
Liposomal Amphotericin B 3 mg/kg IV daily |
| Candida krusei  
(intrinsically resistant to fluconazole) | Micafungin 100 mg IV Daily  
See comment 5 regarding primary use of voriconazole | Transition to voriconazole within 5-7 days is appropriate in patients who are clinically stable, are no longer candidemic, and who have susceptible isolates  
Preferred:  
Voriconazole 6 mg/kg PO/IV q12h x2 doses, then 4 mg/kg PO/IV q12h⁸  
Alternative:  
Liposomal Amphotericin B 3 mg/kg IV daily |
| “Other yeast” | Consult ID | Consult ID |

⁷ Fluconazole should be used with caution in patients with severe renal impairment (serum creatinine >2 mg/dL) due to potential for decreased elimination of the drug.
⁸ If possible, avoid use of Liposomal Amphotericin B in patients with renal impairment (serum creatinine >2 mg/dL) due to potential for increased toxicity.

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**Notes:**
- **Micafungin** is a fungal cell membrane-targeting agent that is active against yeasts and hyphae of Candida species, as well as other fungal species such as *Candida* and *Aspergillus*.
- **Fluconazole** is a triazole antifungal agent that is effective against *Candida* species and is often used as initial therapy for candidemia.
- **Liposomal Amphotericin B** is a form of amphotericin B that is encapsulated in liposomes to improve its delivery and reduce toxicity.
- **Voriconazole** is an azole antifungal agent that is effective against *Candida* species and is often used as an alternative therapy in cases of fluconazole resistance.

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**References:**
EMPIRIC THERAPY FOR SUSPECTED INVASIVE CANDIDIASIS IN ICU PATIENTS

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Primary Therapy</th>
<th>Alternative Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empiric therapy for patients with unexplained fever or other signs of infection and who are at high risk for invasive candidiasis.</td>
<td><strong>Micafungin</strong> 100 mg IV daily</td>
<td><strong>Fluconazole</strong> 800 mg x1 day, then 400 mg IV/PO daily OR <strong>Liposomal Amphotericin B</strong> 3 mg/kg IV daily</td>
</tr>
<tr>
<td>High risk patients are defined as those in the ICU with:</td>
<td>- Discontinuation of empirical antifungal therapy is strongly encouraged in patients with BDG values that are negative (&lt;80 pg/mL). If the initial BDG value is ≥80 pg/mL, a repeat test is recommended as 2 consecutive serum BDG ≥80 pg/mL are suggestive of invasive candidiasis in high-risk patients. However, positive results should not be utilized as the sole evidence for continuation of antifungal therapy, given the poor positive-predictive value of the test. BDG reacts with non-<em>Candida</em> fungi and false positive reactions are also common in ICU patients. Please see <strong>BDG Guidance Document</strong>.</td>
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<tr>
<td><strong>EITHER</strong></td>
<td><strong>Infectious Diseases should be consulted when two positive BDG results are obtained and/or if continuation of empiric therapy is desired in the absence of positive cultures.</strong></td>
<td>See comments 1 and 2 regarding use of fluconazole and Liposomal Amphotericin B</td>
</tr>
<tr>
<td>Recent gastrointestinal perforations/anastomotic leaks (tertiary peritonitis)</td>
<td></td>
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<tr>
<td><strong>OR</strong></td>
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<tr>
<td>Having 2 or more of the following: in the ICU ≥3 days, ventilated, receiving broad spectrum antibiotics, have a central line and have 1 of these additional risk factors: parenteral nutrition, dialysis, major surgery, pancreatitis, receiving steroids or other immunosuppressive agents.</td>
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<tr>
<td>In such patients, a Beta-D-Glucan assay should be performed prior to or with the initiation of empiric antifungal therapy and appropriate cultures should be taken.</td>
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</table>

**Table Comments:**
1. Fluconazole may be considered for patients who are clinically stable and have no recent history of azole antifungal exposure prior to positive cultures.
2. Micafungin-resistant *C. glabrata* is emerging at UMHS. Prior exposure is highly correlated to the development of resistance. In critically ill and neutropenic patients, empirical treatment with liposomal amphotericin B may be preferred in patients with recent exposure to echinocandins.
3. Micafungin should not be used for the treatment of meningitis, or candiduria.
4. Micafungin and systemic amphotericin B are not recommended for the treatment of endophthalmitis due to poor vitreous penetration. Intravitreal antifungal therapy for patients with severe endophthalmitis and vitritis may be necessary. Please see **Ocular Infection Guidelines** for the treatment of *Candida* endophthalmitis.
5. Voriconazole should only be used as empiric therapy if additional coverage of molds is indicated as its spectrum of activity for Candida spp. is similar to fluconazole.
6. Oral voriconazole should be administered on an empty stomach, doses should be rounded to nearest 50 mg increment (Tablet available as 50 and 200 mg strengths; suspension also available).
7. Fluconazole requires dose adjustment in patients with renal insufficiency. Please refer to **Renal Dosing Recommendations**.
8. Voriconazole should be dosed based on adjusted body weight in morbidly obese patients. Please refer to **Weight-Based Dosing in Obese Patients**.


**Antimicrobial Subcommittee Approval:** N/A

**P&T Approval:** 07/2016

**Originated:** Unknown

**Last Revised:** 04/2018

**Revision History:**

*The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider’s professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.*

If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.