## GUIDELINES FOR TREATMENT OF CANDIDEMIA AND CANDIDIASIS IN PEDIATRICS

## **General Recommendations for all patients:**

- Yeast in a blood culture should **NOT** be considered a contaminant
- An 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 in patients with candidemia
- Patients should have a dilated fundoscopic exam performed to rule out endophthalmitis
- Exception: In neutropenic patients, repeat ophthalmological exam should be considered once neutropenia has resolved
- Additional evaluation for metastatic foci (e.g., echocardiogram, renal ultrasound) should be performed for neonates or 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 be treated a minimum of 4-6 weeks

Empiric Therapy for Pediatrics						
Clinical Setting	Primary Therapy	Alternative Therapy	Comments			
Clinically stable Mild to moderate illness	<b>Micafungin</b> 5 mg/kg/dose IV daily (max: 150 mg/dose)	Fluconazole 12 mg/kg/dose IV daily	Patients at high risk of <i>C. krusei</i> or <i>C. glabrata</i> should not receive empiric fluconazole: patients with malignancies, patients with diabetes, patients with a previous history of <i>C. krusei</i> or <i>C. glabrata</i> Micafungin should not be used for meningitis, endocarditis (native or prosthetic), endophthalmitis, OR candiduria			
Clinically unstable Moderate to severe illness	Micafungin 5 mg/kg/dose IV daily (max 150 mg/dose)	Liposomal amphotericin B 5 mg/kg/dose IV daily	Micafungin should not be used for meningitis, endocarditis (native or prosthetic), endophthalmitis, OR candiduria			
DEFINITIVE THERAPY IN PATIENTS WITH POSITIVE BLOOD CULTURES						
Pathogen	First Line Therapy	Alternative Therapy				
Candida albicans Candida dubliniensis Candida parapsilosis Candida tropicalis Candida lusitaniae	<b>Micafungin</b> 5 mg/kg/dose IV daily (max: 150 mg/dose)	For patients with fluconazole-susceptible isolates, transition to fluconazole once clinically stable and no longer candidemic  Preferred: Fluconazole 12 mg/kg/dose IV/PO daily  Alternative (if unable to take or intolerant of azole antifungals): Liposomal Amphotericin B 5 mg/kg/dose IV daily (C. lusitaniae is considered resistant to Amphotericin B)				



Candida glabrata	<b>Micafungin</b> 5 mg/kg/dose IV daily (max: 150 mg/dose)	Transition to fluconazole or voriconazole in patients in whom an oral option is needed once they are clinically stable, are no longer candidemic  Preferred (if fluconazole MIC ≤8):  Fluconazole 12 mg/kg/dose IV/PO daily  Alternative (if fluconazole MIC >8 and voriconazole MIC is ≤0.5):  Voriconazole 7-9 mg/kg/dose IV BID  OR (if unable to take or intolerant of azole antifungals):  Liposomal Amphotericin B 5 mg/kg/dose IV daily	
Candida krusei (intrinsically resistant to fluconazole)	<b>Micafungin</b> 5 mg/kg/dose IV daily (max: 150 mg/dose)	Transition to voriconazole within 5-7 days is appropriate in patients who are clinically stable, are no longer candidemic, and who have voriconazole-susceptible isolates  Preferred: Voriconazole 7-9 mg/kg/dose IV BID  Alternative (if unable to take or intolerant of azole antifungals): Liposomal Amphotericin B 5 mg/kg/dose IV daily	
"Other yeast"	Consult ID	Consult ID	



EMPIRIC THERAPY FOR SUSPECTED INVASIVE CANDIDIASIS					
Clinical Setting	Primary Therapy	Alternative Therapy			
Empiric therapy for patients with unexplained fever or other signs of infection and who are at high risk for invasive candidiasis:  High risk for Candida infection: 1) Invasive Candida infection in the past 6 months  OR 2) ICU-level patient with central venous catheter AND 2 or more of the following: more than 3 days broad spectrum antibiotics in past 2 weeks, TPN, short bowel syndrome, or neutropenia due to chemotherapy or stem cell transplant	Micafungin 5 mg/kg/dose IV daily (max: 150 mg/dose)	Preferred: Fluconazole 12 mg/kg/dose IV/PO daily (for patients who have had no recent azole exposure and not colonized with azole-resistant Candida species)  Alternative (if unable to take or intolerant of azole antifungals): Liposomal Amphotericin B 5 mg/kg/dose daily  *Stop antifungals if no clinical response to therapy in 4-5 days or have no subsequent evidence of invasive candidiasis			
Neonatal Invasive Candidiasis	Amphotericin B deoxycholate 1 mg/kg/dose IV daily (with disseminated candidiasis)  Suspicion of CNS involvement: Liposomal Amphotericin B 5 mg/kg/dose IV daily	*Lumbar puncture and a dilated retinal examination are recommended in neonates with cultures positive for Candida species from blood and/or urine *Computed tomographic or ultrasound imaging of the genitourinary tract, liver, and spleen should be performed if blood cultures are persistently positive for Candida species  Preferred Alternative for Non-CNS Disease: Fluconazole 12 mg/kg/dose IV/PO daily  Alternative: Liposomal Amphotericin B 5 mg/kg/dose daily (use with caution in the presence of urinary tract involvement)  Add on: For patients who have not had a clinical response to initial Amphotericin B therapy, as salvage therapy the addition of flucytosine 25 mg/kg/dose QID may be considered (adverse effects are frequent)  Step-down (after patient responded to initial treatment): Fluconazole 12 mg/kg/dose PO daily  Duration: For patients without obvious metastatic complications - 2 weeks (after clearance of Candida species from the bloodstream and resolution of signs)			

IDSA guidelines recommend fluconazole doses of 12 mg/kg/dose daily for preterm and full-term neonates. However, some experts recommend 12 mg/kg q48h for neonates  $\leq$ 7 days of life and 12 mg/kg q24h for neonates  $\geq$ 8 days of life.



## **Table Comments:**

- 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.
- 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.
- Fluconazole requires dose adjustment in patients with renal insufficiency. Please refer to Renal Dosing Recommendations.

Reference: Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1-50.

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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.

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