

Carolina Antimicrobial Stewardship Program | UNC Hospitals Candida Bloodstream Infection Management

Candidemia is associated with increased morbidity and mortality in hospitalized patients. Prompt, appropriate antifungal therapy is essential to improve outcomes in patients with candidemia. In addition, optimal management of candidemia involves timely removal of indwelling devices and catheters, evaluation for complications associated with candidemia, and treatment considerations related to species, susceptibilities, and patient-specific factors. Standardized, evidence-based approaches to management of *Candida* bloodstream infections have been shown to improve clinical outcomes.^{1,5,8,11} Infectious Diseases consultation is required for patients with candidemia at UNC Medical Center. E-consultation is appropriate for patients at Hillsborough Hospital.



*Fluconazole is an acceptable alternative to an echinocandin as initial therapy for candidemia in select patients (hemodynamically stable, no prior azole exposure, low risk for fluconazole resistance). Risk factors for azole resistance include increased age, underlying malignancy, and diabetes.

Care Management Checklist

- Effective empirical therapy initiated same day as positive microscopy
- Removal of CVC if feasible within 4 days of onset of candidemia
- De-escalation and transition to enteral step-down therapy, if appropriate
- □ Adequate duration of therapy defined

Approved by the UNC Medical Center P&T Committee 12/19/22

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- □ Ophthalmologic exam (or consult)
- Echocardiography
- Follow up blood cultures q 48 hrs to document clearance

Updated July 2023



Drug Selection and Dosing:

- Echinocandin (micafungin) is the recommended empirical therapy for most patients with candidemia.
- Amphotericin B or fluconazole are preferred therapies for neonates with invasive candidiasis due to lack of intact blood-brain barrier. ID consultation is highly recommended.
- Candida species is generally predictive of antifungal susceptibilities in the absence of recent or prior antifungal exposure.
- Voriconazole is recommended as stepdown therapy for patients with candidemia due to *Candida krusei* or other species that are fluconazole resistant. High dose fluconazole strategy (12 mg/kg/day or 800mg daily) should be used for S-DD *Candida glabrata*; recommend ID or ASP consult if considering fluconazole for other S-DD species.
- Obese patients may require higher doses (6 mg/kg/day if normal renal function, 800 mg daily maximum dose)
- For patients with CNS, ophthalmic, or cardiac involvement, or suppurative thrombophlebitis, higher doses of fluconazole are required (12 mg/kg daily dose in patients with normal renal function, 800 mg daily maximum dose). For patients with suspected cardiac involvement or suppurative thrombophlebitis, higher doses of micafungin are recommended (150 mg daily). These patients should receive ID consultation.

Antifungal Dosing for Adults				
	Standard-dose Fluconazole	High-dose Fluconazole	Micafungin	
CrCl ≥ 50 ml/min	800 mg x 1 dose, then 400 mg q24h	800 mg q24h		
CrCl < 50 ml/min	400 mg x 1 dose, then 200 mg q24h	400 mg q24h	100 mg g 24h	
HD	200 mg q24h	400 mg q24h	100 mg q24m	
СVVН	800 mg x 1 dose, then 400-800 mg q24h	800 mg q 24h		
Antifungal Dosing for Pediatric Patients				
	Standard-dose Fluconazole	High-dose Fluconazole	Micafungin	
CrCl <u>></u> 50 ml/min	12 mg/kg x 1 dose (MAX 800 mg), then	12 mg/kg/dose (MAX 800 mg) g24b		
	6 mg/kg/dose g24h (Max 400 mg)	12 mg/kg/d03e (MAX 000 mg/ q24n		
	o mg/ng/acco q= m (max 100 mg)			
CrCl < 50 ml/min	6 mg/kg x 1 dose (Max 400 mg), then	6 ma/ka/dose (Max 400 ma) a24b		

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	Neonates & Infants <90 Days Old (23-40 weeks gestational age and first 90 days of life)	Consult Pediatric Pharmacy for dosing
Precautions with Azole Antifungals:		

- Clinically significant drug interactions exist with azole antifungals including but not limited to tacrolimus, cyclosporine, rifamycins, chemotherapy agents, and antiretrovirals. Consult ASP for recommendations if needed.
- Therapeutic drug monitoring (TDM) may be necessary for voriconazole, itraconazole, and posaconazole therapy. Consult ASP or service pharmacist for assistance with TDM. <u>UNCMC TDM Guideline</u>
- Prolonged azole use in pregnancy is associated with significant risks and should generally be avoided.
- Monitor LFTs at baseline and once weekly for patients receiving azole antifungals.
- Azole antifungals except isavuconazole may prolong the QTc interval. Monitoring may be warranted in certain patients (e.g., prolonged baseline QT, multiple QT prolonging drugs).

Duration of Therapy:

- Without metastatic complications <u>2 weeks of therapy</u> should be given starting from first day of documented negative blood cultures.
- Patients with CNS, ophthalmic, or cardiac involvement, or suppurative thrombophlebitis require longer durations of therapy. These patients should be seen by the ID consult service.

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