

SPECTRA OF ACTIVITY OF ANTIFUNGAL AGENTS (in alphabetical order):

Fungus	Amphotericin B	Fluconazole	Posaconazole	Voriconazole	Echinocandins class
Aspergillus sp.	+ (± for <i>A. terreus</i>)	-	+	+	+
Candida sp.	+	± (<i>C. krusei</i> is resistant; dose-dependent for <i>C. glabrata</i>)	+	+	+ (± for <i>C. parapsilosis</i>)
Cryptococcus sp.	+	+	+	+	-

ANTIFUNGAL REGIMENS AVAILABLE INCLUDE:

Class	Regimens (usual dosing) in alphabetical order by drug		
Azoles	Fluconazole 800 mg IV/PO daily	Posaconazole† 200 mg PO Q6H for invasive fungal infections -200 mg PO TID for prophylaxis in GVHD	Voriconazole 6 mg/kg IV/PO Q12h x2 doses then 4mg/kg IV/PO q12h thereafter for invasive aspergillosis
Echinocandins	Anidulafungin† 200 mg Day 1 then 100 mg IV daily	Caspofungin 70 mg IV Day 1 then 50 mg IV daily	Micafungin† 100 mg IV daily
Polyenes	Amphotericin B deoxycolate 0.5-1 mg/kg IV daily	Liposomal amphotericin 3 mg/kg IV daily	--

†UHN only

For management of **documented** candidemia, please refer to “[ASP Simple Messaging – Candidemia](#)”.

IN WHOM SHOULD EMPIRIC ANTIFUNGALS BE CONSIDERED?

- ✦ In critically ill patients, risk factors for candidemia are:
 - Intra-abdominal sepsis, especially if achievement of source control is uncertain
 - Exposure to broad-spectrum antibiotics
 - Presence of central venous catheter
 - Total parenteral nutrition
 - Renal replacement therapy
 - Exposure to systemic corticosteroid and other cell-mediated immunosuppressive therapy
- ✦ In febrile neutropenic patients, particularly in those with fever for longer than 4d despite appropriate empiric antibiotics.

SELECT INDICATIONS OF SPECIFIC ANTIFUNGALS:

Fluconazole: empiric treatment

- in azole-naïve patients
- in areas where *C. albicans* accounts for the majority of yeast isolates – MSH ICU and TGH CVICU

Voriconazole: empiric treatment of invasive aspergillosis

Posaconazole:

- alternative to liposomal amphotericin and voriconazole in treatment of invasive aspergillosis
- prophylaxis of invasive fungal infections in bone marrow transplant patients with GVHD

Echinocandins:

- Empiric treatment of candidemia
 - in azole-experienced (e.g. fluconazole prophylaxis) patients
 - in areas where non-albicans yeast account for majority of yeast isolates – TWH ICU and TGH ICU
- caspofungin is an alternative to voriconazole and L-AMB for invasive aspergillosis

Amphotericin B deoxycolate: alternative to azoles or echinocandins for candidemia

Liposomal amphotericin (L-AMB):

- alternative to voriconazole in invasive aspergillosis due to progression of disease
- alternative to amphotericin deoxycolate in those at risk of nephrotoxicity (age>50, concomitant nephrotoxic agents, renal insufficiency at baseline)
- treatment of invasive fungal infections involving the CNS

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ADDITIONAL DIAGNOSTIC AND THERAPEUTIC COMMENTS

- ✦ Serum galactomannan twice weekly in high-risk febrile neutropenic patients as surveillance testing for invasive aspergillosis
- ✦ Bronchoscopy ideally within 72h of initiation of empiric antifungal (if not before) to obtain sample for staining and fungal cultures and to rule out other infections in those with suspected invasive aspergillosis.

References:

1. Walsh TJ et al. Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2008;46:327–60.
2. Pappas PG et al. Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48:503–35.

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