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

<table>
<thead>
<tr>
<th>Fungus</th>
<th>Ampytericin B</th>
<th>Fluconazole</th>
<th>Posaconazole</th>
<th>Voriconazole</th>
<th>Echinocandins class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus sp.</td>
<td>+ (± for A. terreus)</td>
<td>-</td>
<td>+</td>
<td>±</td>
<td>+ (± for C. parapsilosis)</td>
</tr>
<tr>
<td>Candida sp.</td>
<td>+</td>
<td>± (C. krusei is resistant; dose-dependent for C. glabrata)</td>
<td>+</td>
<td>±</td>
<td>+ (± for C. parapsilosis)</td>
</tr>
<tr>
<td>Cryptococcus sp.</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

ANTIFUNGALS REGIMENS AVAILABLE INCLUDE:

<table>
<thead>
<tr>
<th>Class</th>
<th>Regimens (usual dosing) in alphabetical order by drug</th>
<th>Fluconazole 800 mg IV/PO daily</th>
<th>Posaconazole† 200 mg PO Q6H for invasive fungal infections</th>
<th>Voriconazole 6 mg/kg IV/PO Q12h x2 doses then 4 mg/kg IV/PO x2 doses for invasive aspergillosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoles</td>
<td>Anidulafungin† 200 mg Day 1 then 100 mg IV daily</td>
<td>Caspofungin 70 mg IV Day 1 then 50 mg IV daily</td>
<td>Micafungin† 100 mg IV daily</td>
<td></td>
</tr>
<tr>
<td>Echinocandins</td>
<td>Amphoterin B deoxycolate 0.5-1 mg/kg IV daily</td>
<td>Liposomal amphoterin 3 mg/kg IV daily</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Polyenes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†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 amphoterin 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

Amphoterin B deoxycolate: alternative to azoles or echinocandins for candidemia

Liposomal amphoterin (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
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