# Adult Antifungal Guidance

**Proven or Presumed Candidaemia**

Empiric treatment prior to identification of species

- Clinically stable patients
  - + Non neutropenic
  - + No recent (within 4 weeks) azole exposure or fluconazole treatment failure
  - + No previous positive blood culture/invasive infection due to azole resistant isolate
  - + No prolonged exposure to azoles
  - + No current colonization with fluconazole resistant Candida species
  - + No intolerance of/contraindication (e.g. drug interaction) to fluconazole

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<tr>
<th>Antifungal</th>
<th>Alternative</th>
<th>Duration</th>
<th>Comments</th>
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| FLUCONAZOLE IV
  800mg loading dose then
  400mg daily maintenance dose |
| Change to ANIDULAFUNGIN or CASPOFUNGIN as per guidance below if clinical deterioration. |
| 2 weeks after first negative blood culture and resolution of symptoms |
| Blood cultures should be repeated every second day until negative |

- If patient was neutropenic: 2 weeks after first negative blood culture and resolution of symptoms and resolution of neutropenia

- If patient was culture negative: For patients who have no clinical response to empiric antifungal therapy at 4–5 days and who do not have subsequent evidence of invasive candidiasis after the start of empiric therapy or have a negative non-culture-based diagnostic assay with a high negative predictive value, consideration should be given to stopping antifungal therapy

**All other patients**

(except oncology and haematology patients – see links in red box above)

- Neutropenic or Non-neutropenic:
  - ANIDULAFUNGIN IV
    - 200mg loading dose then
    - 100mg daily maintenance dose
  - OR
  - CASPOFUNGIN IV (alter dose if Child Pugh score 7-9 unless score driven by hypoalbuminaemia)
    - 70mg loading dose then
    - 50mg daily (≤80kg)
    - 70mg daily (>80kg)
    - 105mg daily (>110kg)
  - Do not use Caspofungin in severe liver impairment (Child Pugh score>9) and/or drug interactions

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| ^AMBISOME IV
  3mg/kg/day (can be increased up to 5mg/kg/day) |
| Prescribe by brand name |
| 2 weeks after first negative blood culture and resolution of symptoms |
| Blood cultures should be repeated every second day until negative |

- Central line removal/replacement is recommended as it can act as a reservoir. Remove any implicated prosthetic material unless absolutely contra-indicated.

- Consider dilated fundoscopy to exclude endophthalmitis and investigations to rule out infective endocarditis

**FLUCONAZOLE/CASPOFUNGIN – always check for drug interactions**

Fluconazole IV is significantly cheaper than Anidulafungin and Caspofungin IV

**ALWAYS DISCUSS WITH ID OR MICROBIOLOGY PRIOR TO PRESCRIBING OF IV ANTIFUNGALS**

- These guidelines apply to invasive infections in non pregnant adults only. See separate guidelines for oncology and haematology patients.
- Invasive fungal infections are mostly seen in non-neutropenic intensive care patients and in haematology/oncology patients with neutropenia or immunosuppression.
- Voriconazole offers no advantage over fluconazole for isolates that are sensitive to both of these azole antifungals.
- Refer to voriconazole professional checklist and patient alert card [here](http://www.fungalpharmacology.org/ or [https://antifungalinteractions.org/](https://antifungalinteractions.org/)
- Always check for interactions in SPC or consult pharmacist or specialist website - [http://www.fungalpharmacology.org/](http://www.fungalpharmacology.org/) or [https://antifungalinteractions.org/](https://antifungalinteractions.org/)
<table>
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<tr>
<th>CANDIDAEMIA targeted treatment following identification of species</th>
<th>Candida glabrata/ Candida krusei isolated</th>
<th>ANIDULAFUNGIN IV 200mg loading dose then 100mg daily maintenance dose OR CASPOFUNGIN IV (alter dose if Child Pugh score 7-9 unless score driven by hypoalbuminaemia) 70mg loading dose then 50mg daily (&lt;80kg) 70mg daily (&gt;80kg) 105mg daily (&gt;110kg) Do not use Caspofungin in severe liver impairment (Child Pugh score&gt;9) and/or drug interactions</th>
<th>♠AMBISOME IV 3mg/kg/day (can be increased up to 5mg/kg/day) Prescribe by brand name</th>
<th>As above</th>
<th>As above</th>
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<tr>
<td>Candida albicans isolated</td>
<td>FLUCONAZOLE IV (dosing as above)</td>
<td>CASPOFUNGIV IV or ANIDULAFUNGIN IV</td>
<td>As above</td>
<td>As above</td>
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<tr>
<td>Candida parapsilosis isolated</td>
<td>FLUCONAZOLE IV (dosing as above)</td>
<td>♠AMBISOME IV 3mg/kg/day (can be increased up to 5mg/kg/day) Prescribe by brand name</td>
<td>As above</td>
<td>As above</td>
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<td>CANDIDA in urine</td>
<td><strong>Check sensitivities and consult with ID/Microbiology before initiating treatment.</strong> Treat high risk patients including neutropenic or those undergoing urologic manipulation/instrumentation</td>
<td>FLUCONAZOLE IV (dosing as above) High concentrations in urine</td>
<td>FUNGIZONE IV Prescribe by brand name. Dosing as per p5 below. <strong>DO NOT USE AMBISOME.</strong> Consider adding FLUCYTOSINE IV/PO Note: check with pharmacy re stock before prescribing. Supply issues with IV and PO is unlicensed</td>
<td>Review at 7 days</td>
<td>AMBISOME, other azoles and echinocandins cannot be used as they do not reach adequate levels in urine. Consider removal of prosthetic material (catheter/nephrostomy etc) if possible. Flucytosine – see cryptococcal section below re levels</td>
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<td><strong>INVASIVE ASPERGILLOSIS OR SUBACUTE INVASIVE ASPERGILLOSIS (SAIA)</strong></td>
<td><strong>ANTIFUNGAL</strong></td>
<td><strong>ALTERNATIVE</strong></td>
<td><strong>DURATION</strong></td>
<td><strong>COMMENTS</strong></td>
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<td><strong>VORICONAZOLE</strong> IV 6mg/kg every 12 hours for 2 doses then 4mg/kg every 12 hours. Consider switch to oral if patient clinically responding, able to tolerate and absorb oral medication. Bioavailability of oral voriconazole is 96%.</td>
<td>If patient is intolerant of IV voriconazole use AMBISOME 3mg/kg/day (can be increased up to 5mg/kg/day). <strong>Prescribe by brand name</strong> or ISAVUCONAZOLE 200mg tds for 2 days then 200mg od Oral POSACONAZOLE* or ISAVUCONAZOLE may be an alternative switch in patients unable to tolerate voriconazole.</td>
<td>Minimum of 6-12 weeks</td>
<td>Always check for drug interactions with VORICONAZOLE, ISAVUCONZAOLE and POSACONAZOLE* Ensure voriconazole (1.3 - 5.5mg/L)/posaconazole (1-3.75mg/L) predose level is checked within 5 days of commencing therapy and when any interacting drugs are commenced / discontinued. See SPC re warning about accumulation of intravenous vehicle for IV VORICONAZOLE in patients with renal impairment Ensure patient has voriconazole alert card *Posaconazole liquid and tablets are not interchangeable – always specify formulation on prescription and check dosage.</td>
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<th><strong>HAEMATOLOGY/ONCOLOGY PATIENTS</strong></th>
<th>See separate guidance</th>
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| **RESPIRATORY PATIENTS**  
Chronic Pulmonary Aspergillosis (CPA), Allergic Bronchopulmonary Pulmonary Aspergillosis (ABPA), Severe Asthma with Fungal Sensitisation (SAFS)** | See separate guidance |
|---|---|

| **MUCORMYCOSIS** | Consult ID/Microbiology, start AMBISOME IV 5mg/kg/day (Brain involvement or solid organ transplant or refractory disease use 10mg/kg /day) **Prescribe by brand name.**  
Consider IV isavuconazole 200mg tds for 2 days then 200mg od as alternative in renal disease, progressive disease or toxicity with Ambisome. In stable disease or partial response switch to oral isavuconazole or posaconazole tablets. TDM required for posaconazole (pre dose 1-3.75 mg/L) and should be considered for isavuconazole (pre dose 1-4mg/L) in some clinical situations such as suspected treatment failure, drug interactions, suspected toxicity or intolerance, obesity, or after switching from IV to oral therapy in a patient with documented mucormycosis.  
If rhino-orbital disease seek urgent surgical opinion for consideration of debridement. Echinocandins (caspofungin/andidulafungin) and Voriconazole are not active against this infection. | | |
### CRYPTOCOCCAL MENINGITIS

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<tr>
<th>HIV patients</th>
<th>See separate guidance for <a href="#">Treatment of Opportunistic Infections</a></th>
<th>Echinocandins (caspofungin/anidulafungin) do not have activity against <em>Cryptococcus</em> spp.</th>
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<tbody>
<tr>
<td>Transplant patients/Non HIV patients</td>
<td>Induction: ³AMBISOME IV 4mg/kg + FLUCYTOSINE PO 25mg/kg/every 6 hours (if oral route not available use fluconazole IV 800mg daily)</td>
<td>IV Flucytosine has been discontinued in the UK</td>
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<td>Consolidation: FLUCONAZOLE PO 400-800mg/day</td>
<td>PO Flucytosine is not licensed for use in the UK d/w pharmacist to obtain supply</td>
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<td>Maintenance: FLUCONAZOLE PO 200mg/day</td>
<td>Haematological/hepatic toxicities are associated with high blood levels - flucytosine levels (pre dose and 2 hour post dose) should be done 3-5 days after starting therapy and after any changes in renal function).</td>
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³AMBISOME - Initial test dose of 1mg should be given over 10 minutes, stop infusion and observe patient for at least 30 mins, continue if no anaphylactoid/allergic reactions. Test dose has to be repeated at beginning of each new course of treatment. Always prescribe by brand name. Avoid slow escalation of doses. Use lean body weight in obese patients.

#### References:
1. [IDSA Candidiasis Guidelines 2016](#)
2. [IDSA Management of Cryptococcal Disease Guidelines 2010](#)
3. [IDSA Treatment of Aspergillosis Guidelines 2016](#)
4. [ESCMID Candida Guidelines 2012](#)
5. [British Society for Medical Mycology Invasive Fungal Infections 2003](#)
6. [UKCPA Drug dosing in Extremes of Body Weight 2013](#)
7. [Expert Local Opinion](#)
8. JA Roberts et al; Drug Dosing in Obesity; published 2017
9. Wurtz et al; Antibiotic Dosing in Obese Patients; Clin Inf Dis; 1997
10. Mourad et al; Tolerability profile of the current antifungal armoury; JAC; 2018
11. Pea et al; Overview of antifungal dosing in invasive candidiasis; JAC; 2018
12. [SAPG Candidaemia Guidance 2019](#)
13. [Global for the diagnosis and management of mucormycosis 2019](#)
FUNGIZONE Infusion Information Sheet
Must be prescribed by brand name

General:

- Normally only used for fungal urinary tract infections.
-Always flush line/cannula before and after each dose and dilute Fungizone with 5% glucose.
- Fungizone should never be flushed with or reconstituted with 0.9% sodium chloride as they are incompatible.
- A 1mg test dose must be administered at the beginning of each new course of treatment
- Fungizone infusion should be a final concentration of 1mg/10ml.
- Infusions should be used immediately after dilution and protected from light.
- Fungizone vials are kept in the fridge.
- To reduce nephrotoxicity 1 litre of 0.9% sodium chloride should be infused over 1-2 hours (according to patient’s age and clinical status) prior to each dose of Fungizone.
- Electrolytes especially Mg and K, renal function, FBC, LFTs should be monitored daily.
- The maximum dose is 1.5mg/kg/day. In critically ill patients consider starting with day 2 dosing below.
- Pharmacist: If no buffer is available check pH of glucose batch with Baxter Medicines Information Department (or other manufacturer) to ensure above 4.2 then no requirement for buffer.

Day 1 – Dose: 0.5 mg/kg = __________ mg

Dosing weight: use Actual body weight in all patients including obesity (but check with pharmacist)

- Reconstitute each vial of Fungizone with 10ml sterile water for injection and shake immediately until clear. (Concentration of resulting solution is 5mg/ml).
- Add the contents of 1 vial of buffer for amphoteracn to __________ ml bag of glucose 5%.
- Withdraw __________ mls and add to buffered infusion bag.
- For test dose infuse __________ mls (1mg) over 20-30 minutes, stop infusion and observe patient for further 30 minutes. Continue if no anaphylactoid/allergic reactions.
- Infuse the rest of the bag over 2-4 hours or up to 6 hours if necessary.
- If patient complains of ‘flu like’ symptoms decrease the rate of the infusion.

Day 2 – Dose: Consider increasing dose to 1mg/kg depending on severity and toxicity

Day 3 – Dose: Normal daily dose is up to 1mg/kg. In seriously ill patients up to 1.5mg/kg has been used. Discuss with ID/Micro/Pharmacy.