NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Invasive Candidiasis in non haemato oncology adult patients

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Approval Group:	Antimicrobial Utilisation Committee

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Guidelines for the treatment of invasive candidiasis in non-haemato-oncology adult patients

NHS Greater Glasgow and Clyde

Proven invasive candidiasis
OR
Yeast seen on Gram stain of blood culture or normally sterile fluid
(See notes 1, 2 & 3 overleaf)

1. Remove central venous catheters present at the time of positive blood culture, unless absolutely contraindicated. If a line cannot be removed, discuss management with an infection specialist (microbiology or infectious diseases).
2. **If patient has <u>new</u> visual symptoms** or if the patient non-verbal, and in all ICU patients, request referral to Ophthalmology for advice/opinion.
3. Remove any implicated prosthetic material (e.g. ureteric stent, biliary stent, V-P shunt), unless absolutely contraindicated.
4. Repeat blood cultures daily, until negative.

⇨

DO ANY OF THE FOLLOWING APPLY?

- Septic/unstable patient with *Candida* isolate of unknown species identification/susceptibility.
- Previous (within 4 weeks) positive blood culture/invasive infection due to an azole-resistant isolate.
- Recent (within 4 weeks) failure of fluconazole.
- Currently colonised with fluconazole-resistant *Candida* species/infection with *C. glabrata* of unknown fluconazole susceptibility.
- Intolerance of/contraindication (e.g. drug interaction) to fluconazole.

YES → **Caspofungin IV** * (Also see notes 4 & 5 overleaf)

Loading dose, all patients: 70mg on day 1

Maintenance dose (from day 2 onwards):
Weight ≤ 80 kg: 50mg once daily
Weight > 80 kg: 70mg once daily
<u>Moderate</u> hepatic impairment (Child-Pugh score 7-9): 35mg once daily, regardless of weight

Notes

- No dose 🡻 is needed in renal impairment/renal replacement therapy or in <u>MILD</u> hepatic impairment (Child-Pugh score 5-6). There is no information available for <u>SEVERE</u> hepatic impairment (Child-Pugh score >9); use ANIDULAFUNGIN instead (refer to product literature for dosing/prescribing advice).
- The maintenance dose may need increased if caspofungin is co-administered with enzyme inducers (see product literature).
- Monitor LFTs (seek advice if these deteriorate).

---------- OR ----------

AmBisome® IV * ^ (Also see notes 4 & 5 overleaf)

Initial test dose: 1mg over 10 min, stop infusion and observe patient for at least 30 mins, continue if no anaphylactoid/allergic reactions. If anaphylactoid/ allergic reactions stop immediately & <u>DO NOT</u> continue
Starting dose (in non-neutropenic patients):
1 mg/kg/day (as a single dose over 30-60 min) increasing to 3 – 5 mg/kg/day (5 mg/kg/day dose unlicensed) depending on response.

Neutropenic patients: discuss antifungal choice/dose with an infection specialist.

Notes
Monitor renal function. No dose 🡻 is necessary in renal impairment/ renal replacement therapy.

NO → **Fluconazole IV** * ❖ (Also see notes 4 & 5 overleaf)

Loading dose, all patients:
800mg on day 1 (as a single dose over 40 min).

Maintenance dose (from day 2 onwards):
Depends on fluconazole sensitivity. Either -
C*andida* species shown to be sensitive on testing:
400 mg/day (as a single dose, over 20 min).
OR
***Candida* species with dose-dependent sensitivity**:
800 mg/day (as single dose, over 40 min).

Renal impairment
[NB. see Therapeutics Handbook for calculation of Creatinine Clearance (CrCl)]

- **CrCl ≥ 10 ml/min** dose as normal renal function (Renal Drug Handbook, different dosing from SPC)
- **CrCl < 10 ml/min** reduce dose of fluconazole by 50%

Renal replacement therapy

- CAPD/HD: reduce dose of fluconazole by 50%
- CVVH/CVVHD: no dose reduction

Footnotes:
* Consult the BNF/product literature for detailed prescribing advice.

^ Amphotericin B deoxycholate (i.e. non-lipid formulation amphotericin B) is **NOT RECOMMENDED**.

❖ There are **numerous drug interactions with fluconazole** (& other azole antifungal drugs). Pharmacy can advise on the significance & management of these.

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Notes

1. Prophylactic, empirical and pre-emptive antifungal treatment

There are no multicentre randomised controlled clinical trials in adult patients to support the use of prophylactic, empirical or pre-emptive antifungal therapy in non-neutropenic patients. Locally agreed (with microbiology) and validated algorithms identifying high risk patients who may benefit from these approaches may be employed.

Empirical therapy – discuss with microbiology.

May be justified in patients with continuing fever or sepsis despite >72 hours broad-spectrum antibiotics and no obvious source of the infection. Risk factors to consider include: CVC/TPN; length of stay >3 days; multiple broad-spectrum antibiotics; haemodialysis; GI perforation/surgery; *Candida* colonisation at >1 site. **Endotracheal colonisation alone is not an indication for empiric therapy.** If treating empirically use fluconazole 800mg IV on day 1 as loading dose, followed by IV 400mg/day as a maintenance dose (as a single dose).

2. European Organisation for Research and Treatment of Cancer (EORTC) definition of proven invasive fungal disease

***Microscopic analysis of sterile material*:**

Histopathologic, cytopathologic, or direct microscopic examination of a specimen obtained by needle aspiration or biopsy from a normally sterile site (other than mucous membranes) showing yeast cells *e.g. Candida* species showing pseudohyphae or true hyphae.

***Culture*:**

(i) Recovery of a yeast by culture of a sample obtained by a sterile procedure (including a freshly placed [≤24 hours ago] drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process.
(ii) Blood culture that yields *Candida* species.

Where *Candida* species is cultured from a line tip:

(i) If evidence of systemic infection, treat according to guideline.
(ii) If no evidence of infection, observe and seek microbiology advice if infection develops.

3. Exclusions from management algorithm

(i) Localised syndromes such as infective endocarditis, meningitis, septic arthritis, osteomyelitis, prosthetic device infections, renal tract candidiasis or retinitis/endophthalmitis caused by *Candida* species. Treatment of such conditions should be carried out in consultation with a microbiologist.
(ii) Superficial candidiasis, unless presenting as a skin manifestation of disseminated candidiasis.

4. Step-down therapy

Discuss step-down timing, antifungal choice and dosing with microbiology. Oral fluconazole should be used as step-down therapy for fluconazole sensitive and dose-dependent sensitive *Candida* isolates.

NB. There are numerous drug interactions involving fluconazole. Pharmacy can advise on the significance & management of these.

5. Treatment duration

Assuming complete clinical/microbiological resolution and in the absence of localised syndromes (see Note 3(i) above), antifungal therapy should be continued for 14 days after blood cultures become negative. Where candidiasis arises from a removable source (*e.g.* vascular catheter, ureteric stent) treatment should be continued for 14 days after removal of the source. If recovery is delayed or there is evidence of refractory disease, the choice of antifungal therapy and its duration should be discussed with a microbiologist.