# Invasive Fungal Disease in Adults; Prophylaxis, Investigation, and Treatment - Microbiology Summary Clinical Guideline

Reference number: CG-T/2023/216

## Primary prophylaxis

### Yeast (Candida species)

Antifungal prophylaxis is recommended when the incidence of *Candida* IFD is ≥ 6
%. In specific populations of haematology and oncology patients, antifungal prophylaxis against *Candida* species is recommended.

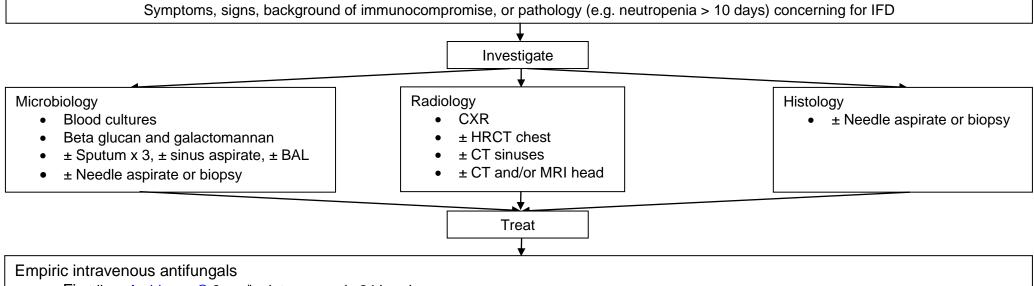
## Yeast (Candida species) and mould (Aspergillus species)

 Antifungal prophylaxis is recommended when the incidence of Aspergillus IFD is ≥ 6 %. In specific populations of haematology and oncology patients, antifungal prophylaxis against Candida and Aspergillus species is recommended.

#### **Primary prophylaxis table** (with neutropenia [< 0.5 x 10<sup>9</sup> neutrophils/I])

Diagnoses and therapies	Prophylaxis	Duration
Chronic lymphocytic leukaemia (CLL)	No prophylaxis	
CLL + geriatric or advanced and unresponsive disease or neutropenia > 6 months	± Prophylaxis	
Chronic myeloid leukaemia (CML). Tyrosine kinase inhibitor	No prophylaxis	
Lymphoma. No intensive chemotherapy	No prophylaxis	
Myelodysplastic syndrome. No intensive chemotherapy	No prophylaxis	
Myeloma	No prophylaxis	
Autologous HSCT with mucositis anticipated preengraftment	Fluconazole	From initiation to 7 days after resolution of neutropenia
Lymphoma. Intensive chemotherapy	Fluconazole	From initiation to 7 days after resolution of neutropenia
Solid tumour + mucositis anticipated for ≥ 7 days + neutropenia	Fluconazole	From initiation to 7 days after resolution of neutropenia
Acute myeloid leukaemia. Intensive chemotherapy	Posaconazole	From initiation to 7 days after resolution of neutropenia
Allogeneic HSCT	Posaconazole	Engraftment, or post HSCT day 75
Aplastic anaemia, severe	Posaconazole	From initiation to 7 days after resolution of neutropenia
Autologous HSCT; neutropenia > 14 days or slow engraftment anticipated or failure of engraftment	Posaconazole	Engraftment, or post HSCT day 75
CML. Intensive chemotherapy	Posaconazole	From initiation to 7 days after resolution of neutropenia
Graft versus host disease + prednisolone (or equivalent) $\ge$ 1 mg/kg per day for > 1 week + neutrophils < 1 x 10 <sup>9</sup> /l for > 1 week	Posaconazole	Graft versus host disease resolved, or prednisolone (or equivalent) < 10 mg/day
Graft versus host disease + prednisolone (or equivalent) ≥ 2 mg/kg per day for > 2 weeks	Posaconazole	Graft versus host disease resolved, or prednisolone (or equivalent) < 10 mg/day
Myelodysplastic syndrome. Intensive chemotherapy	Posaconazole	From initiation to 7 days after resolution of neutropenia
Acute lymphocytic leukaemia. Intensive chemotherapy	Ambisome®	From initiation to 7 days after resolution of neutropenia





- First line: <u>Ambisome®</u> 3 mg/kg intravenously 24 hourly
- Second line options:

 <u>Posaconazole</u> 300 mg intravenously 12 hourly for the first 24 hours, and 300 mg intravenously 24 hourly thereafter NB Posaconazole's empiric antifungal spectrum includes *Candida* species, *Cryptococcus* species, *Aspergillus* species, and Mucorales

Caspofungin. If ≥ 81 kg, 70 mg intravenously 24 hourly. If < 81 kg, 70 mg intravenously for the first 24 hours, and 50 mg intravenously 24 hourly thereafter</li>

NB Caspofungin's empiric antifungal spectrum includes *Candida* species and *Aspergillus* species; however, there is no anti-cryptococcal activity, and anti-Mucorales activity is limited to a putative, synergistic role in dual therapy with Ambisome®

Review microbiology, radiology, and/or histology criteria re proven, probable, and/or possible IFD

POSITIVE

 Candidiasis/cryptococcosis/aspergillosis/mucormycosis management, including directed antifungals NEGATIVE

• Consider ceasing empiric antifungal treatment in collaboration with the medical senior/consultant

NB Please note, this guidance relates especially to Candida species, Cryptococcus species, Aspergillus species, and Mucorales. If the differential diagnosis includes pneumocystosis, please note <u>Pneumocystis jirovecii</u> hospital guidelines

#### **References**

**Bennett, J. E., et al.** 2015. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8<sup>th</sup> Edition. Elsevier.

British National Formulary. 2023. BNF.

**Cornely, O. A., et al.** 2014. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. Clinical Microbiology and Infection.

**De Pauw, B., et al.** 2008. Revised Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clinical Infectious Diseases.

**Donnelly, J. P., et al.** 2020. Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium, Clinical Infectious Diseases.

Johns Hopkins ABX Guide. 2019. Cryptococcal Meningitis. Available at: Cryptococcal Meningitis | Johns Hopkins ABX Guide (hopkinsguides.com).

**Maertens, J. A., et al.** 2018. European guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommendations from the European Conference on Infections in Leukaemia. Journal of Antimicrobial Chemotherapy.

**Pappas, P. G., et al.** 2016. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases.

**Sanford Guide Antimicrobial Therapy.** 2022. Cryptococcosis. Available at: <u>https://www.sanfordguide.com/products/digital-subscriptions/</u>.

**Schelenz, S., et al.** 2015. British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases. The Lancet.

**The Renal Drug Database.** 2019. The Renal Drug Handbook, 5<sup>th</sup> Edition. CRC Press.

**Ullmann, A. J., et al.** 2018. Diagnosis and management of *aspergillus* diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline. Clinica Microbiology and Infection.

**Wingard, J. R.** 2021. Prophylaxis of invasive fungal infections in adult hematopoetic cell transplant recipients. UpToDate. Available at: <u>Prophylaxis of invasive fungal</u> infections in adult hematopoietic cell transplant recipients - UpToDate.

**Wingard, J. R.** 2022. Prophylaxis of invasive fungal infections in adults with hematologic malignancies. UpToDate. Available at: <u>Prophylaxis of invasive fungal infections in adults with hematologic malignancies - UpToDate</u>.

# **Document control**

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