Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust

South Yorkshire and Bassetlaw

Antifungal Guidelines for adult patients

Approved by Drug & Therapeutics Committee:	November 2022, updated July 2026
Implementation Date:	July 2026
Review Date:	July 2028

Scope and exceptions

This guideline applies to:

Setting	Trust – Doncaster and Bassetlaw Teaching Hospitals
Individuals	Medical, Non-medical prescribers, Nursing and Pharmacy staff
Speciality	Antimicrobial Therapy

This guideline does not apply to:

Neonates

1. Summary and guideline

1. Contents

2. Introduction

This guideline is divided into 3 sections

1. Prophylactic therapy aimed at preventing fungal infection in patients deemed to be at sufficient risk
2. Empiric therapy in patients suspected but not confirmed to have fungal infection including guidance as to appropriate laboratory tests to confirm or refute the diagnosis
3. Targeted therapy when fungal infection has been confirmed

This guideline is intended to be a living document replacing local trust guidelines where possible but reviewing and integrating changes to regional guidelines as and when they occur. Any such remaining or new antifungal guidelines should have a member of the antifungal stewardship team on the authorship or review panel to ensure consistency between documents across the trust.

Interim annual review of this guideline will be performed by the antifungal stewardship team with full review on a 3-yearly basis or earlier where significant change dictates.

Antifungal advice can be sought from Consultant in Infection.

Therapeutic drug monitoring is essential for management in instances with the hyperlink TDM. Details can be found in appendix 3.[1]

Many of the antifungal agents, particularly the azoles, have multiple important drug interactions. Please consider these where relevant when prescribing.

Drug Susceptibility considerations

Candida

Approximately 75% of confirmed invasive Candida infections locally are due to the species *C. albicans, C. dubliniensis, C. parapsilosis* or *C. tropicalis,* which are usually susceptible to fluconazole unless the patient has received antifungals in the recent past. Where other species are isolated from significant infections please liaise with Microbiology if necessary to determine the appropriate therapeutic strategy.

Mould infections

The majority of confirmed mould infections are due to *Aspergillus spp.* The vast majority of clinical isolates in the UK remain susceptible to mould active azoles (e.g. voriconazole, posaconazole, isavuconazole) but reduced susceptibility has been noted in up to 25% of isolates in the Netherlands and is also more common in patients with a long history of exposure to mould-active azoles. Susceptibility testing is performed by the reference laboratory – please contact Microbiology at the time of sample acquisition/culture confirmation to discuss if drug resistance is a concern.

Invasive infections caused by non-aspergillus moulds are rare and, where suspected, management should occur in conjunction with Microbiology.

Pneumocystis jirovecii

Co-trimoxazole remains first line therapy for *Pneumocystis*. Although strains with reduced susceptibility have been recognised, evidence suggests that this resistance is overcome by the high doses of drug used in this context. Routine susceptibility testing is not possible due to the non-cultivable nature of *P. jirovecii.*

3. Prophylaxis

A consensus antifungal prophylaxis risk table developed on behalf of NHS England can be found in appendix 2.

Antifungal prophylaxis in haematology patients

Clinical Indication	Drug dose and route	Duration
Autologous stem cell transplant	Fluconazole 100mg PO once daily	Days –1 until count recovery
Allogeneic stem cell transplant	Mould active prophylaxis (see below)	Days -1 to +100 or while on immunosuppression for Graft vs Host Disease whichever is the longest
Graft vs Host Disease requiring steroids or other immunosuppression	Mould active prophylaxis (see below)	Duration of Immunosuppression
Acute Myeloid Leukaemia (AML) and Myelodysplastic Syndrome (MDS) during induction and salvage chemotherapy	Mould active prophylaxis (see below)	Until neutrophil count recovery AND complete remission
AML and MDS during consolidation chemotherapy	Consider Mould active prophylaxis (see below)	During consolidation chemotherapy
Acute Lymphoblastic Leukaemia (ALL) induction	Prophylaxis not routinely indicated – alternate day caspofungin may be considered in some patients by lymphoid malignancy consultant	No prophylaxis
ALL salvage	Mould active prophylaxis (see below)	During salvage chemotherapy
Intensively treated Chronic Myeloid Leukaemia (high dose Thymidine Kinase	Mould active prophylaxis (see below)	During chemotherapy

Inhibitor or AML type regimens)		
Severe aplastic anaemia (as per British Society for Haematology definition)	Mould active prophylaxis (see below)	Until neutrophil count recovery
Intensive or dose-escalated chemotherapy for lymphoma	Prophylaxis not routinely indicated. Fluconazole 100mg PO once daily may be considered in some patients by lymphoid malignancy consultant	For duration of chemotherapy
CAR-T cell therapy	Mould active prophylaxis (see below)	Day -5 to +28 (or recovery of neutrophil count to >1, whichever is longer) then switch to fluconazole until CD4 count >200

Mould active prophylaxis

1st line

- Posaconazole tablets 300mg twice daily on the first day then 300mg daily thereafter. N.B tablets and suspension dose are not interchangeable

Alternatives

- Posaconazole suspension – 200mg three times a day . Therapeutic drug monitoring is mandatory.[TDM]
- Alternate day caspofungin is occasionally used in patients intolerant or unable to receive azoles but its evidence base is currently slim.

3.2 Antifungal prophylaxis in Oncology

Clinical Indication	Drug dose and route	Duration
Specified docetaxel containing regimens	Fluconazole 50mg PO once daily	7 days duration from day 5 of chemotherapy

3.3 Antifungal prophylaxis in Surgical patients[2]

Clinical Indication	Drug dose and route	Duration
Severe Acute Pancreatitis (modified Glasgow score of 3 or greater) or CT evidence of necrosis	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV/PO once daily.	10 days
Oesophageal rupture	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily.	5 days post drainage/repair assuming clinical stability
GI perforation or anastomotic leak in the context of recent antibacterial therapy (usually repeat laparotomy)	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily.	5 days post washout/repair assuming clinical stability

The requirement for antifungal prophylaxis in this context will be reviewed over the current lifespan of this document now that in-house beta-D-glucan testing has become available

3.4 Antifungal prophylaxis in Hepatology[3]

Clinical Indication	Drug dose and route	Duration
Acute liver failure with encephalopathy requiring ITU admission	Fluconazole 400mg* (or 6mg/kg if >70kg up to a maximum of 800mg) IV once daily	Duration of requirement for level 3 care for encephalopathy

The requirement for antifungal prophylaxis in this context will be reviewed over the current lifespan of this document now that in-house beta-D-glucan testing has become available

3.5 Antifungal prophylaxis in Immunology patients

Patients with a variety of uncommon or rare primary and secondary immune deficits are at risk of fungal disease. Decisions about prophylaxis in this group should align with guidelines in other groups and will be made on the recommendation of an Immunology Specialist on consultation with Microbiology where required.

3.6 Pneumocystis jirovecii prophylaxis

Pneumocystis jirovecii prophylaxis is recommended in those patients with an estimated risk of disease of >3%. A lower threshold for prophylaxis may be adopted in patients with previous *Pneumocystis* pneumonia

Clinical Indication	Drug dose and route	Duration
Pneumocystis jirovecii prophylaxis	1st line Co-trimoxazole 480mg PO twice a day three times a week on Mondays, Wednesdays and Fridays OR 480mg PO od. 2nd line Atovaquone 750mg PO twice a day*	Duration of immunocompromise – suggested durations in common clinical contexts listed below.

*Prophylactic use of atovaquone is an unlicensed indication.

Duration of *Pneumocystis* prophylaxis:

- HIV with CD4 count <200x10^6/L or CD4 percentage <14%
- Steroid therapy equivalent to 20mg prednisolone per day for >4 weeks
- Renal Transplant patients for 6 months after transplant (or 1 year if total lymphocyte count <1x10^9/L at 6 months)
- Acute Lymphoblastic Leukaemia on chemotherapy (excluding during high dose methotrexate, unless at consultants' discretion)
- During and for 6 months following completion of purine analogue therapy
- Ibrutinib, Idelalisib, Acalabrutinib or Zanubrutinib therapy- consider on case by case basis.
- During treatment with CAMPATH and ATG
- Autologous transplants = 3 months
- Autologous transplant + TBI = 6 months
- Allogeneic transplant = 12 months
- Post donor lymphocyte infusions = 3 months
- GVHD whilst active GVHD or on treatment for GVHD
- CAR-T cell receptors= 6-12 months (d-5 until CD4 count >200.)

- Patients undergoing treatment with anti-BCMA or anti-GPRC5D immunotherapies
- Small cell and non-small cell lung cancer patients receiving concurrent chemoradiotherapy

4. Empiric therapy

4.1 Empiric antifungal therapy in patients with neutropenic sepsis

Clinical Indication	Drug dose and route	Notes
Neutropenic sepsis without clear focus and with persisting fever after ~96hrs antibacterials	Caspofungin 70mg IV loading dose, then 50mg once a day IV if ≤80kg or 70mg once a day IV if >80kg	• Request HRCT scan within 24 hours • Consider bronchoscopy • Send fungal serology (BD Glucan and Galactomannan) • Discuss with Microbiology

4.2 Empiric antifungal therapy in suspected invasive candidiasis[4]

Clinical Indication	Drug dose and route	Notes
Suspected **non-urinary tract** invasive candidiasis. Consider especially in: • Abdominal disease and recent broad spectrum antibiotic use • Invasive devices who have failed to respond to broad spectrum antibiotics	Anidulafungin 200mg IV on day 1 then 100mg IV once a day	• Send blood cultures and BD glucan • Consider appropriate imaging and source control • Discuss with Microbiology
Suspected urinary tract source invasive candidiasis	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily.	Other azoles and echinocandins DO NOT penetrate urinary tract well • If fluconazole resistant Candida UTI suspected (see above) contact Microbiology • Send blood cultures, urine and BD glucan • Consider urinary tract imaging

4.3 Empiric therapy in suspected invasive mould infection[5]

The majority of invasive mould infections occur in profoundly immunocompromised Haemato-oncology patients but a smaller number of cases are diagnosed in other patient groups including critically ill patients with influenza or COVID-19

Clinical Indication	Drug dose and route	Notes
Suspected invasive aspergillosis (consistent clinical picture and consistent changes on CT)	Voriconazole 6mg/kg IV twice a day on day 1 then 4mg/kg twice a day . Therapeutic drug monitoring is mandatory. TDM Monitor LFT See below if voriconazole not tolerated	• Bronchoscopy where possible including fungal culture and BAL galactomannan • Send serum galactomannan • Liaise with Microbiology about sampling and about alternatives if prior azole exposure • Monitor LFT
If invasive non-Aspergillus mould infection suspected	Liaise with Microbiology	

Where patients are critically ill with presumed invasive aspergillosis, it may be reasonable to add anidulafungin or caspofungin to the voriconazole until therapeutic levels are attained – discuss with Microbiology or the antifungal stewardship team.

2nd line mould active agents

If voriconazole not tolerated due to adverse effects, or if therapeutic levels difficult to achieve then consider:

- Isavuconazole 200mg tds (IV/PO) for 6 doses then 200mg once a day. The infusion requires the use of an in-line 0.2 - 1.2micron polyethersulfone (PES) filter
- Liposomal amphotericin B 3mg/kg IV once a day (higher doses of up to 10mg/kg used if suspected mucoraceous mould (zygomycete) infection).
- Posaconazole 300mg tablets twice daily on the first day then 300mg daily thereafter. TDM N.B tablets and suspension dose are not interchangeable.

5. Treatment of confirmed infection

For treatment of dermatophytosis and complex organ-specific fungal infection (e.g. CNS, eye, endovascular, bone and joint, endocarditis) contact Microbiology or refer to specialty specific guidelines.

5.1 Candidiasis[4]

5.1.1 Oral and oesophageal candidiasis

Clinical Indication	Drug dose and route	Duration and notes
Oral candidiasis	Nystatin 100 000 units four times a day PO OR miconazole oral gel 2%, 2.5mL four times a day	7 days
Oral candidiasis with failed response to nystatin or in heavily immunocompromised	Fluconazole 100mg once a day PO. OR Fluconazole 150mg stat PO may be used in a palliative care context.	7 days. • Consider swab • Contact Microbiology if confirmed/suspected fluconazole resistant organism
Oesophageal candidiasis	Fluconazole 200-400mg once a day PO	14-21 days • Contact Microbiology if confirmed/suspected fluconazole resistant organism

5.1.2 Genital candidiasis

Clinical Indication	Drug dose and route	Duration and notes
External genital candidiasis	Fluconazole 150mg stat PO OR Clotrimazole 1% cream applied to affected area 2-3 times daily	STAT 7 days
Vaginal candidiasis	Fluconazole 150mg stat PO OR Clotrimazole pessary 200mg nightly PV	STAT 3 nights
Genital candidiasis with failed response to clotrimazole	Fluconazole 150mg stat PO	Stat dose • Consider swab if recurrent • Contact Microbiology if confirmed/suspected fluconazole resistant organism
Recurrent vulvovaginal candidiasis	Nystatin 100 000 unit pessaries nightly for 12-14 days (Note: available in packs of 12 pessaries) Boric acid 600mg pessaries nightly for 14 days Suppressive therapy with Fluconazole 150mg 3x/week then weekly for 6 months if fluconazole susceptible	Consider alternative dermatological differential diagnoses e.g. lichen sclerosus or contact dermatitis and systemic predisposing factors such as HIV, diabetes mellitus or iron deficiency anaemia Advise avoidance of irritants e.g. soaps or perfumes Note: Nystatin and boric acid pessaries are unlicensed products but have been approved for use at DBTH.

5.1.3 Urinary tract candidiasis

Clinical Indication	Drug dose and route	Duration and notes
Asymptomatic candiduria	Treatment not usually indicated	Often represents contamination or colonisation of catheter if present. If treatment indicated e.g. due to forthcoming surgery then follow UTI guidance below
Lower UTI - Fluconazole susceptible isolate	Fluconazole 200mg once a day	7-14 days Other azoles and echinocandins DO NOT penetrate urinary tract well.
Lower UTI - Fluconazole resistant isolate	Contact Microbiology	
Upper UTI - Fluconazole susceptible isolate	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV/PO once daily.	At least 14 days Other azoles and echinocandins DO NOT penetrate urinary tract well
Upper UTI - Fluconazole resistant isolate	Contact Microbiology	

* Options include fluconazole dose increase; addition of second systemic agent, 5-flucytosine alone or in combination or conventional amphotericin depending on patient and organism factors.

5.1.4 Respiratory tract candidiasis

Respiratory tract candidiasis is extremely uncommon and most isolates from sputum or BAL fluid represent contamination by oral flora. Please contact Microbiology if genuine infection suspected.

5.1.5 Abdominal candidiasis related to surgery or perforated viscus

Clinical Indication	Drug dose and route	Duration and notes
Fluconazole susceptible isolate	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily. Oral step-down on advice of Microbiology	At least 14 days depending upon effectiveness of source control and clinical progress. Monitoring of BD glucan may be helpful
Fluconazole resistant isolate	Anidulafungin 200mg IV on day 1 then 100mg IV once a day. Oral step-down where possible on advice of Microbiology	

5.1.6 Candida bloodstream infection

Clinical Indication	Drug dose and route	Duration and notes
Treatment of Candida bloodstream infection before species known	Anidulafungin 200mg IV on day 1 then 100mg IV once a day	14 days treatment after first negative blood culture • Repeat blood cultures on alternate days until negative • Remove all intravenous lines • Exclude endocarditis and endophthalmitis (echocardiogram and fundoscopy. Ophthalmology review if visual change or patient unable to confirm otherwise e.g. sedated patients).
Treatment of Candida bloodstream infection due to fluconazole susceptible isolate after initial 5 days echinocandin therapy and if fit the following criteria: - Haemodynamically stable - Repeat blood culture remains negative - Non-neutropenic - Any identified source controlled	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily Oral step-down on advice of Microbiology	
Treatment of Candida bloodstream infection due to fluconazole resistant isolate	Anidulafungin 200mg IV on day 1 then 100mg IV once a day Oral step-down where possible on advice of Microbiology	

5.1.7 Candida from line tips

Culture of Candida species from intravascular line tip samples can represent genuine infection or contamination of the sample from the exit site on withdrawal.

Clinical Indication	Drug dose and route	Duration and notes
Fluconazole susceptible isolate	Fluconazole 800mg on day 1 then 400mg (or 6mg/kg if >70kg up to maximum of 800mg) IV once daily Oral step-down on advice of Microbiology	Send blood culture and beta-d-glucan. Treatment can be stopped at 7 days if culture and BD glucan negative. If either culture or BD glucan positive then treat as candidaemia, above.
Fluconazole resistant isolate	Anidulafungin 200mg IV on day 1 then 100mg IV od Oral step-down where possible on advice of Microbiology	

5.1.8 Candida endocarditis

Clinical Indication	Drug dose and route	Duration and notes
Empirical therapy for presumed Candida endocarditis	Anidulafungin 200mg IV daily (unlicenced dose – as per IDSA Clinical Guideline for the Management of Candidiasis)* **OR** Liposomal amphotericin B 3-5mg/kg once a day IV +/- 5-flucytosine 25mg/kg four times a day PO (i.e. total 100mg/kg/day) . Therapeutic drug monitoring is essential for efficacy and safety TDM of flucytosine.	Management should be in liaison with Microbiology and the infective endocarditis MDT. Treatment should be for at least 6 weeks, generally requires valve replacement and is often followed by long term suppressive therapy *Approved for use in DBTH for this indication in line with Unlicensed medicine policy

5.1.9 Disseminated candidiasis (formerly 'hepatosplenic candidiasis') in haematology patients

Clinical Indication	Drug dose and route	Notes
Disseminated candidiasis (AKA hepato-splenic candidiasis)	Caspofungin 70mg IV loading dose, then 50mg once a day IV if ≤80kg or 70mg once a day IV if >80kg	• Monitor BD glucan

5.2 Cryptococcal meningitis

Clinical Indication	Drug dose and route	Duration/Notes
Cryptococcal meningitis	INDUCTION Liposomal amphotericin B 4mg/kg once a day IV **PLUS** 5-flucytosine 25mg/kg four time a day PO (i.e. total 100mg/kg/day) Therapeutic drug monitoring is essential for efficacy and safety TDM of flucytosine. MAINTENANCE Fluconazole 400 mg once a day PO	Induction course of at least 2 weeks as determined by clinical response and rate of CSF sterilisation. Maintenance 10 weeks Secondary prophylaxis may be indicated if ongoing immunocompromise

5.3 Aspergillus infection[5]

Clinical Indication	Drug dose and route	Duration/Notes
Invasive pulmonary or sinus aspergillosis	Voriconazole 6mg/kg IV twice a day on day 1 then 4mg/kg twice a day. Therapeutic drug monitoring is mandatory. TDM Conversion to PO on discussion with Microbiology or Antimicrobial Pharmacist	6-12 weeks Monitor LFT Combination echinocandin therapy may be considered initially until levels adequate Consider surgery, especially for sinus disease Consider reducing immunosuppression where possible Secondary prophylaxis may be indicated if ongoing immunocompromise
CNS aspergillosis	Voriconazole 6mg/kg IV twice a day on day 1 then 4mg/kg twice a day . Therapeutic drug monitoring is mandatory. TDM	6-12 weeks Monitor LFT Consider surgery Consider reducing immunosuppression where possible Secondary prophylaxis may be indicated if ongoing immunocompromise
Chronic cavitatory pulmonary aspergillosis	• Itraconazole 200mg twice a day solution PO. Therapeutic drug monitoring is mandatory. TDM **OR** • Voriconazole 400mg twice a day PO for 2 doses then 200mg twice a day . Therapeutic drug monitoring is mandatory. TDM	6 months Monitor LFT

Saprophytic aspergilloma	Initial observation and no therapy if not enlarging If Surgical resection performed and concern re: potential for spillage: Voriconazole 6mg/kg IV twice a day on day 1 then 4mg/kg twice a day . Therapeutic drug monitoring is mandatory. TDM	Perioperative treatment only Monitor LFT
Allergic bronchopulmonary aspergillosis	• Itraconazole 200mg twice a day solution PO. Therapeutic drug monitoring is mandatory. TDM **OR** • Voriconazole 400mg twice a day PO for 2 doses then 200mg twice a day. Therapeutic drug monitoring is mandatory. TDM	Where antifungal treatment is indicated under supervision of respiratory specialist.

2nd line mould active agents

If voriconazole is not tolerated due to adverse effects, or if therapeutic levels difficult to achieve then consider:

- Isavuconazole 200mg three times a day (IV/PO) for 6 doses then 200mg once a day. The infusion requires the use of a filter.
- Liposomal amphotericin B 3mg/kg IV once a day (higher doses of up to 10mg/kg used if suspected mucoraceous mould (zygomycete) infection).
- Posaconazole 300mg tablets twice daily on the first day then 300mg daily thereafter. TDM
  N.B tablets and suspension dose are not interchangeable.

5.4 Other mould infection

Contact Microbiology to discuss management of non-Aspergillus mould infection

5.5 Pneumocystis jirovecii pneumonia

Clinical Indication	Drug dose and route	Duration/Notes
Pneumocystis jirovecii pneumonia	1st line Co-trimoxazole 30mg/kg four times a day IV/PO (120mg/kg total daily dose). Dose can be reduced to 90mg/kg/day total from day 4) 2nd line Clindamycin 600mg four times a day IV + primaquine 30mg once a day PO (**Exclude G6PD deficiency**) 3rd line (mild-moderate disease) Atovaquone 750mg twice a day PO	• 21 days total therapy • Consider steroids if hypoxic. (Prednisolone 40mg bd for 5 days, then 40mg od for 5 days, then 20mg od for 11 days if initial pO2 is <9.3kPa on air) • Consider addition of caspofungin as synergistic therapy (70mg load then 50mg od if ≤80kg; 70mg od if >80kg) • See Appendix 5 for important safety considerations before prescribing co-trimoxazole. • Exclude G6PD deficiency before prescribing primaquine • Primaquine is not licensed within the UK. • Secondary prophylaxis may be indicated if ongoing immunocompromise

Appendix 1 – Microbiology and Antimicrobial Pharmacist contact list

Contact Consultant in Infection via the microbiology secretaries
DRI: 01302-642831 or 642835
BDGH: 01909 572490

Contact Antimicrobial Pharmacist via 01302 644325

Appendix 2 – NHS England consensus antifungal prophylaxis risk table

See NHSE Antifungal Stewardship Implementation Pack

Consensus between national guidelines for prophylaxis risks

NHS England

High Risk - mould active prophylaxis	Low Risk - candida prophylaxis	Low Risk - no prophylaxis
Allo-HSCT **Intensive treatment for ALL, AML, MDS** **Significant GVHD** –till resolved. **CML intensive chemo** **Severe aplastic anaemia** Duration Allografts to day 75-100 GVHD – 16 weeks or until prednisolone <10mg OD Others – neutrophil recovery	**Auto-SCT** – candida prophylaxis if mucositis or recent excessive chemo until neutropenia resolved **Myeloma** – fluconazole or no prophylaxis **Lymphoma** - intensive/dose-escalated therapy **Solid tumours** – if profound neutropenia and mucositis expected to last for ≥ 7 days in environments with > 10% risk of invasive Candida infection	**MDS** – not undergoing intensive chemo **CML** (treated with TKIs or conventional treatment) **CLL** No prophylaxis (consider in CLL with prolonged neutropenia (>6 months), elderly, advanced and unresponsive disease) **Lymphoma** - standard chemo **Other myeloproliferative neoplasms**
Unclear		
Autograft – mould-active agent if prior IA, neutropenia >2 weeks expected or prolonged neutropenia prior to HSCT **Allo-HSCT** with expected neutropenia <14 days (II, A) **Aplastic anaemia** - Consider prophylaxis for first months after ATG and after HSCT for as long as neutropenia and/or lymphopenia is present **Allogeneic HSCT** with expected neutropenia >14 days Corticosteroids >1 mg/kg prednisolone equivalent and neutrophils <1 × 10 9 /L for >1 week Corticosteroids >2 mg/kg prednisolone equivalent >2 weeks High-dose cytarabine Fludarabine use in highly treatment-refractory patients with CLL or low-grade lymphoma Alemtuzumab use, especially in highly treatment-refractory patients with CLL or lymphoma		

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Appendix 3 – Therapeutic Drug Monitoring[1,7]

Send a clotted sample of blood (usually a gold top tube) Please ensure Microbiology are aware if the patient is on more than one antifungal as some of these drug levels are meas

red by bioassay

Antifungal	Timing	Sampling Commencement and Frequency	Target Levels/Comments
Itraconazole (oral)	Random (ideally pre-dose, but due to long half-life, random levels are acceptable) **Essential for management of invasive disease**	*Commence:* only after steady state has been reached i.e.1-2 weeks on oral therapy. *Frequency:* dependent on patient and levels achieved - seek advice	**Prophylaxis: 0.5-4.0mg/L** **Therapy: 1.0-4.0mg/L** Contact Antimicrobial Pharmacists for advice in patients on IV therapy
Voriconazole	Pre-dose (i.e. 12 hours post-dose for standard twice a day regimens) **Essential in all cases**	*Commence:* on day 4 of therapy *Frequency:* until therapeutic levels obtained. Repeat if a dose change, interaction or a question of poor compliance and 2-4 weekly thereafter	**Pre dose 1.0-5.5mg/L or 2.0-5.5 mg/L for bulky or disseminated infections** If dosage changes are required, discuss with the Antimicrobial Pharmacists Due to the non-linear kinetics of the drug, informed clinical judgement regarding target range is not possible on any sample except pre-dose samples
Posaconazole	Random (ideally pre-dose, but due to long half-life, random levels are acceptable) **Essential for management of invasive disease.**	*Commence:* only after steady state has been reached i.e.1-2 weeks on oral therapy *Frequency:* once or twice early in course. Repeat if required to check compliance, or if possible drug interaction	**Prophylaxis: 0.7-3.75mg/L** **Therapy: 1.0 -3.75mg/L**

Isavuconazole	Pre-dose	Test if clinical concern about drug exposure (e.g. malabsorption), or failure of response. Commence after 3 days of therapy Discuss subsequent testing with Microbiology	Target levels not yet established and informed clinical judgement is required for dose adjustments. Normal range on standard 200mg od therapy at steady state is **2-4 mg/L** Dose escalation is advised for any level less than 1mg/L
5-Flucytosine	Pre- and post- (2 hours post oral or 30 mins post IV) dose **Essential in all cases**	Within 72 hours of therapy initiation then repeated at least weekly. Repeat within 72 hours of dose adjustment or modification of interacting drugs or renal function	**Pre-dose: 20-50mg/L** **Post-dose: 50-100mg/L**

Appendix 4 – Dose adjustments for hepatic and renal dysfunction

See corresponding monograph here – A-Z Antimicrobial Drug Monographs (sharepoint.com)

Or consult product literature. Home - electronic medicines compendium (emc)

Appendix 5 – High-dose Co-trimoxazole in the treatment of PCP: Important safety considerations

Adverse Effects & Monitoring:
High-dose Co-trimoxazole may cause bone marrow suppression, renal impairment, and electrolyte disturbances—particularly hyperkalaemia. Rarely, it may cause serious skin reactions such as SJS, TEN or DRESS with eosinophilia– the highest risk period is the first week of treatment.

Folate Considerations:

- Check serum folate ideally before starting treatment; do not delay antibiotic initiation while awaiting results.
- Folic acid supplementation does not compromise Co-trimoxazole efficacy[1].
- Initiate folic acid treatment in patients with confirmed folate deficiency.

- Consider folic acid supplementation in at-risk groups, including elderly patients, those with chronic alcohol use, rheumatoid arthritis, malnutrition, or other conditions predisposing to deficiency.

Monitoring Requirements:

Inpatients (clinically unstable)

- FBC, renal function, and U&Es should be monitored ***more frequently than the twice-weekly schedule***, guided by clinical judgement.
- Monitor urine output to reduce the risk of crystalluria (rare), with increased risk in malnourished patients.

Inpatients (clinically stable) and Outpatients

- Twice weekly FBC, renal function, and U&Es

Interaction Precautions:

- Assess for potential drug–drug interactions before starting therapy. For a full list see BNF/SPC.
    - *Methotrexate* – Co-trimoxazole may increase free plasma levels of methotrexate. Both drugs are anti-folate, which increases the risk of bone marrow suppression and pancytopenia. Concurrent use should be avoided.
    - *ACE inhibitors, angiotensin receptor blockers, and potassium-sparing diuretics* – Concurrent use may result in clinically significant hyperkalaemia. Potassium should be monitored closely.
    - *Diuretics (especially thiazides in elderly patients)* – There is a potential increased risk of thrombocytopenia with or without purpura. The manufacturer provides no specific recommendation.
    - *Digoxin* – Co-trimoxazole may increase plasma digoxin levels in elderly patients. Monitor for symptoms of digoxin toxicity such as nausea, anorexia, or visual disturbances, and check serum digoxin levels.
    - *Phenytoin* – Co-trimoxazole may prolong the half-life of phenytoin, resulting in increased serum levels. Monitor for toxicity symptoms including confusion, blurred vision, nystagmus, ataxia, or drowsiness, and adjust the dose if necessary.
    - *Warfarin* – Co-trimoxazole may increase the anticoagulant effect of warfarin. Monitor the INR and adjust the warfarin dose accordingly.
    - *Sulfonylureas (such as gliclazide)* – Hypoglycaemia has been rarely reported. Increase blood glucose monitoring and adjust antidiabetic drug doses if necessary.
- Pay particular attention to medications recently discontinued, such as Methotrexate. Due to its pharmacokinetics, Methotrexate may persist in the body for several months after cessation[2], increasing the risk of additive toxicity when combined with Co-trimoxazole.

Escalation Pathways:

- Suspected myelosuppression: Liaise with Haematology for management of bone marrow suppression, including consideration of folinic acid treatment. Consult Microbiology for alternative antimicrobial options if needed.
- Renal impairment: Consult ward pharmacist for renal dose adjustment.

- Hyperkalaemia: Initiate treatment and consider alternative therapy in discussion with Microbiology.

Reference:

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2. STH Acute Pancreatitis interdisciplinary guideline, 2011
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3. Version history

Version	Date issued	Brief summary of changes	Author
Version Number	Date	Summary of changes	Author (first name & last name)
3 (Previous versions on old format)	November 2025	• Updated to new STH format. • Clarified duration of prophylaxis for CAR-T cell therapy patients and AML patients.	Dr David Partridge (Consultant Microbiologist) Callum Saxon (Antimicrobial Pharmacist)

		• Clarified fluconazole dosing in all indications to bring in line with licensing. • Anidulafungin has replaced fluconazole as first line therapy for 4.2 empiric antifungal therapy in suspected invasive candidiasis • Removed reference to Ambisome as now replaced with generic liposomal amphotericin B, removed need for test dose as per licensing. • Clarified required filters for administration where appropriate. • Added criteria for treated of fluconazole susceptible candida bloodstream infection. • Removed reference to IV flucytosine as no longer available, oral formulation is available. • Updated contacts, linked appendix 4 with live and updated monographs	

4. Document imprint