Document Control

Title

Antifungal Prophylaxis for Haematology and Oncology Patients Guideline (Shared with RDE)

Author	**Author's job title** Consultant Medical Microbiologist (RD+E) Consultant Haematologist (RD+E / NDDH) Consultant Medical Microbiologist (NDDH) Antibiotic Pharmacist (NDDH)
Directorate Planned Care	**Department** Microbiology

Version	Date Issued	Status	Comment / Changes / Approval
0.1	Jul 2019	Draft	Adopted guideline from RD+E with amendments as per CQUIN antifungal stewardship implementation pack.
1.0	Jul 2019	Final	Approved by DTC 18th July with minor amendment to posaconazole re: tablet dose removed and wording to indicate different bioavailability / local NDDH stock inserted instead.

Main Contact Microbiology Department North Devon District Hospital Raleigh Park Barnstaple, EX31 4JB	**Tel: Direct Dial** – **Tel: Internal** – **Email**:
Lead Director Director of Medicine	
Superseded Documents	

Issue Date	Review Date	Review Cycle
Jul 2019	Jun 2022	Three years

Consulted with the following stakeholders:

- Consultant Haematologists
- Consultant Oncologists
- Acute Oncology Nurses
- Acute Haematology Nurses

Approval and Review Process

- Antibiotic Working Group
- Drug & Therapeutics Group

Local Archive Reference
G:\ANTIBIOTICSTEWARDSHIP
Local Path
G:\ANTIBIOTIC STEWARDSHIP\Stewardship\Antibiotic policies\Published policies
Filename
Antifungal Prophylaxis in Haem Onc Adults v1.0 180719

Policy categories for Trust's internal website (Bob) Pharmacy, Microbiology, Haematology, Cancer Services	**Tags for Trust's internal website (Bob)** Antifungal, cancer, leukaemia, immunosuppressed, neutropenia

CONTENTS

1. Purpose

1.1. This document is a shared guideline between the Royal Devon and Exeter NHS Foundation Trust and Northern Devon Healthcare NHS Trust. It specifies how patients should be risk assessed, and which antifungal agents should be used preferentially when prescribing antifungal prophylaxis in adult patients with haematological / oncological conditions.

1.2. This guideline applies to all adults and must be adhered to. Special considerations exist for pregnant and breastfeeding patients; liaise with specialist clinicians as appropriate in these cases. See separate guidance for paediatric patients.

1.3. Non-compliance with this guideline may be for valid clinical reasons only. The reason(s) for non-compliance must be documented clearly in the patient's notes.

1.4. This guideline is primarily aimed at all prescribing teams but other staff (e.g. nursing staff, pharmacists) may need to familiarise themselves with some aspects of the guideline.

1.5. Implementation of this guideline will ensure that:

- Antifungal prophylaxis is managed according to current evidence and standards of practice in the wider healthcare community.
- A standard of care is specified to facilitate a consistent approach between haematology/oncology, microbiology and pharmacy in terms of patient management, specimen processing and drug availability.

2. Responsibilities

2.1. Responsibility for education and training lies with the Lead Consultant Microbiologist for Antibiotic Stewardship. It will be provided through formal study days and informal training on the ward.

2.2. The author will be responsible for ensuring the guidelines are reviewed and revisions approved by the Drug and Therapeutics Group in accordance with the Document Control Report.

2.3. All versions of these guidelines will be archived in electronic format by the author within the Antibiotic Stewardship policy archive.

2.4. Any revisions to the final document will be recorded on the Document Control Report.

2.5. To obtain a copy of the archived guidelines, contact should be made with the author.

2.6. Monitoring of implementation, effectiveness and compliance with these guidelines will be the responsibility of the Lead Clinician for Antibiotic Stewardship. Where non-compliance is found, the reasons for this must have been documented in the patient's medical notes.

Role of Antibiotic Working Group (AWG)

2.7. The AWG is responsible for:

- Leading antibiotic guideline development and review within Northern Devon Healthcare Trust
- Involving all relevant stakeholders in guideline development and review

3. Contacts

3.1. Contact numbers:

• Microbiologist	Bleep 193. Via switchboard out of hours.
• Antibiotic Pharmacist	Bleep 029 (Mon-Fri only)

4. Management of Antifungal Prophylaxis

4.1. See appendix 1

5. Monitoring Compliance with and the Effectiveness of the Guideline

Suggested audit criteria

5.1. The following could be used:

- Using correct risk assessment criteria when making decisions about prescribing antifungal prophylaxis
- Using preferred antifungal prophylaxis agents
- Overall antifungal spend per year

Process for Implementation and Monitoring Compliance and Effectiveness

5.2. Incidents involving antifungal prophylaxis should be reported according to the Trust's Incident Reporting Policy. Critical incident reports relating to antifungal prophylaxis will be collated by the Antibiotic Pharmacist. Results will be reported on an annual basis to the Drug and Therapeutics Group.

6. Equality Impact Assessment

6.1. The author must include the Equality Impact Assessment Table and identify whether the policy has a positive or negative impact on any of the groups listed. The Author must make comment on how the policy makes this impact.

Table 1: Equality impact Assessment

Group	Positive Impact	Negative Impact	No Impact	**Comment**
Age	X			Separate guidance for paediatrics
Disability			X	
Gender			X	
Gender Reassignment			X	
Human Rights (rights to privacy, dignity, liberty and non-degrading treatment)			X	
Marriage and civil partnership			X	
Pregnancy		X		Some treatment advice may harm the unborn foetus, discuss on a case-by-case basis with Obstetricians and Pharmacy for advice.
Maternity and Breastfeeding		X		Some treatments may be excreted in breast milk. Discuss on a case-by-case basis with Paediatricians and Pharmacy for advice.
Race (ethnic origin)			X	
Religion (or belief)			X	

7. References

7.1. Whitney, L; Hall, N; Leach, M. 2018. Improving Value in Specialised Services: Antifungal Stewardship Implementation Pack. NHS England. https://www.england.nhs.uk/wp-content/uploads/2019/03/PSS1-Meds-Optimisation-trigger-5-Antifungal-Stewardship-Implementation-Pack.pdf

7.2. Kerr, P; Porter, R. 2017. Royal Devon and Exeter NHS Foundation Trust Antifungal Prophylaxis Guidelines. https://webview.rx-guidelines.com/Viewing/Index/171#nCghKxSfjb

7.3. British National Formulary [online] via www.new.medicinescomplete.com

7.4. Maertens, JA; Girmenia, C; Brüggemann, RJ; Duarte, R; Kibbler, CC; Ljungman, P; Racil, Z; Ribaud, P; Slavin, MA; Cornely, OA; Donnelly, PJ; Cordonnier, C. On behalf of the European Conference on Infections in Leukaemia (ECIL). 2018. European Guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommendations from the European Conference on Infections in Leukaemia. J Antimicrob Chemother 73: 3221-3230 doi:10.1093/jac/dky286

8. Associated Documentation

- Incident reporting policy
- Antibiotic guidelines for management of neutropenic sepsis
- Antibiotic prescribing policy
- Invasive fungal infections policy

9. Appendix 1 – Antifungal Prophylaxis for Haem/Onc Adults

9.1. Name of guideline on app

Antifungals for Haem/Onc Adults

9.2. Location on app

Secondary Care
Infection
Prophylaxis (surgical and other)
Antifungals for Haem/Onc Adults

9.3. Header

Avoid azole antifungals when using vinca-alkaloids or cyclophosphamide in chemotherapy regimens. Consider instead:

- ⇨ Aerosolized liposomal amphotericin 10mg twice weekly with oral fluconazole 400mg OD (ECIL-3 BII grading).
- ⇨ Low-dose IV liposomal amphotericin (ECIL-3 CI grading) – usually 1mg/kg/day, but alternate regimens include 2mg/kg three times a week, or 7.5mg/kg once weekly.

Tyrosine kinase inhibitors and azoles interact – avoid combination, if necessary use second line after alternatives.

24 hour washout period is advised between anthracycline chemotherapy and azole use due to potential interaction

9.4. High Risk – Mould active prophylaxis [closed]

Patients classed as high-risk: Allogeneic-HSCT; undergoing intensive treatment for ALL, AML, MDS; significant GVHD; undergoing intensive chemotherapy for CML; severe aplastic anaemia; autograft with history of previous invasive fungal infection or prolonged neutropenia expected

- With graft, or failure/cannot tolerate itraconazole
  - Posaconzaole **suspension** 200mg TDS PO (advise to take with food or a fatty meal)
  - NB. Patients from Exeter or out of area may be taking posaconazole 300mg tablets – these have different bioavailability and doses are not equivalent to suspension. Ask for own to be brought in from home if possible, or switch to suspension at dose as above.

- No graft, or failure/cannot tolerate posaconazole
  - Itraconazole oral solution 2.5mg/kg BD PO

Before commencing:

- Rule out pre-existing liver disease, perform baseline LFTs (itraconazole and posaconazole).
- Assess for heart failure (itraconazole).
- Measure serum electrolytes and correct if necessary (posaconazole)
- If any abnormalities present in pre-treatment testing, decision to treat should be based on individual risk:benefit analysis and doses optimised where appropriate.

Monitoring on treatment:

- liver enzyme testing
- plasma drug levels
- Serum electrolyte testing (posaconazole)

Continue until myeloid reconstitution after intensive treatment, allografts continue to day 90-100 OR until cessation of immunosuppressive therapy, GVHD continue 16 weeks OR until prednisolone <10mg OD OR until resolved, other conditions – continue until neutrophil recovery

9.5. Low Risk – for *Candida* prophylaxis only [closed]

Patients classed as usually only requiring *Candida* prophylaxis: Autologous-SCT if mucositis or recent excessive chemotherapy; multiple myeloma; lymphoma if undergoing intensive or dose-escalated therapy; solid tumours if profound neutropenia and mucositis expected to last ≥7 days in environments with >10% risk of invasive *Candida* infection

- Oropharyngeal Candida / mucositis prophylaxis
  - Nystatin 1mL QDS PO
- Systemic Candida prophylaxis if history of extensive thrush or thrush develops on nystatin prophylaxis:
  - Fluconazole 50mg OD PO (if treating initially, may need larger dose for short course before continuing at 50mg daily)

9.6. Previous Invasive Fungal Disease [closed]

- Recommended agent used for prophylaxis will depend on previous isolates – contact microbiology to discuss.

9.7. Prolonged Neutropenia [closed]

Any patient likely to be neutropenic (≤0.5 x 10^9) for ≥10 days

- 1st Line
  - Itraconazole oral solution 2.5mg/kg BD
- 2nd Line
  - Posaconzaole **suspension** 200mg TDS (advise to take with food or a fatty meal)
  - NB. Patients from Exeter or out of area may be taking posaconazole 300mg tablets – these have different bioavailability and doses are not equivalent to suspension. Ask for own to be brought in from home if possible, or switch to suspension at dose as above.

Before commencing:

- Rule out pre-existing liver disease, perform baseline LFTs (itraconazole and posaconazole).
- Assess for heart failure (itraconazole).
- Measure serum electrolytes and correct if necessary (posaconazole)
- If any abnormalities present in pre-treatment testing, decision to treat should be based on individual risk:benefit analysis and doses optimised where appropriate.

Monitoring on treatment:

- liver enzyme testing
- plasma drug levels
- Serum electrolyte testing (posaconazole)

Continue until end of at-risk period

9.8. Assess need for prophylaxis on a case-by-case basis [closed]

- Autograft – provide mould-active agent (posaconazole/itraconazole) if prior IA, neutropenia >2 weeks expected or prolonged neutropenia prior to HSCT
- Allo-HSCT with expected neutropenia <14 days
- 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 >1mg/kg prednisolone equivalent and neutrophils <1 x 10^9/L for >1 week
- Corticosteroids >2mg/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

9.9. Low Risk – No Prophylaxis usually required [closed]

- MDS usually no prophylaxis - unless undergoing intensive chemotherapy
- CML being treated with TKIs or conventional treatment
- CLL usually no prophylaxis – unless any of the following: consider prophylaxis if prolonged neutropenia >6 months, elderly, advanced and unresponsive disease
- Lymphoma on standard chemotherapy
- Other myeloproliferative neoplasms