Ashford and St. Peter's Hospitals
NHS Foundation Trust

Febrile Neutropenia and Non-neutropenia in Paediatric Oncology Patients

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Guideline History		
Date	**Comments**	**Approved By**
02/07/2021	Created: Dr Lojein Hatahet	Paediatric Guideline Committee
13/11/2024	Incorporated CCLG Low Risk pathway, and febrile non-neutropenic initial pathway	Paediatric Guideline Committee
10/06/2026	Addition of pathway for fever in children post treatment for cancer	Paediatric Guideline Committee

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The purpose of the guideline:

The guideline has been designed to clarify the management of febrile neutropenia in immunocompromised patients. All information and guidance are taken from the CCLG guideline.

Background to Fever in Neutropenia (FN):

Neutropenic patients are at risk of rapidly developing life-threatening sepsis. Neutropenic sepsis is a medical emergency. Failure to recognise and treat this condition appropriately may result in unnecessary morbidity and mortality.

All children with a risk of neutropenia who develop a fever (≥ 38.0C) should be assessed in hospital and a first dose of antibiotics given within 60 minutes.

Patients who are at risk of Febrile Neutropenia:

1. All children undergoing anticancer treatment.
2. All children within 6 months of completing cancer treatment
3. Any patient who had HSCT (haematopoietic stem cell transplantation) in the past 12 months must be treated as febrile neutropenia guidelines irrespective of neutrophil count

Definition of "Neutropenic Sepsis"

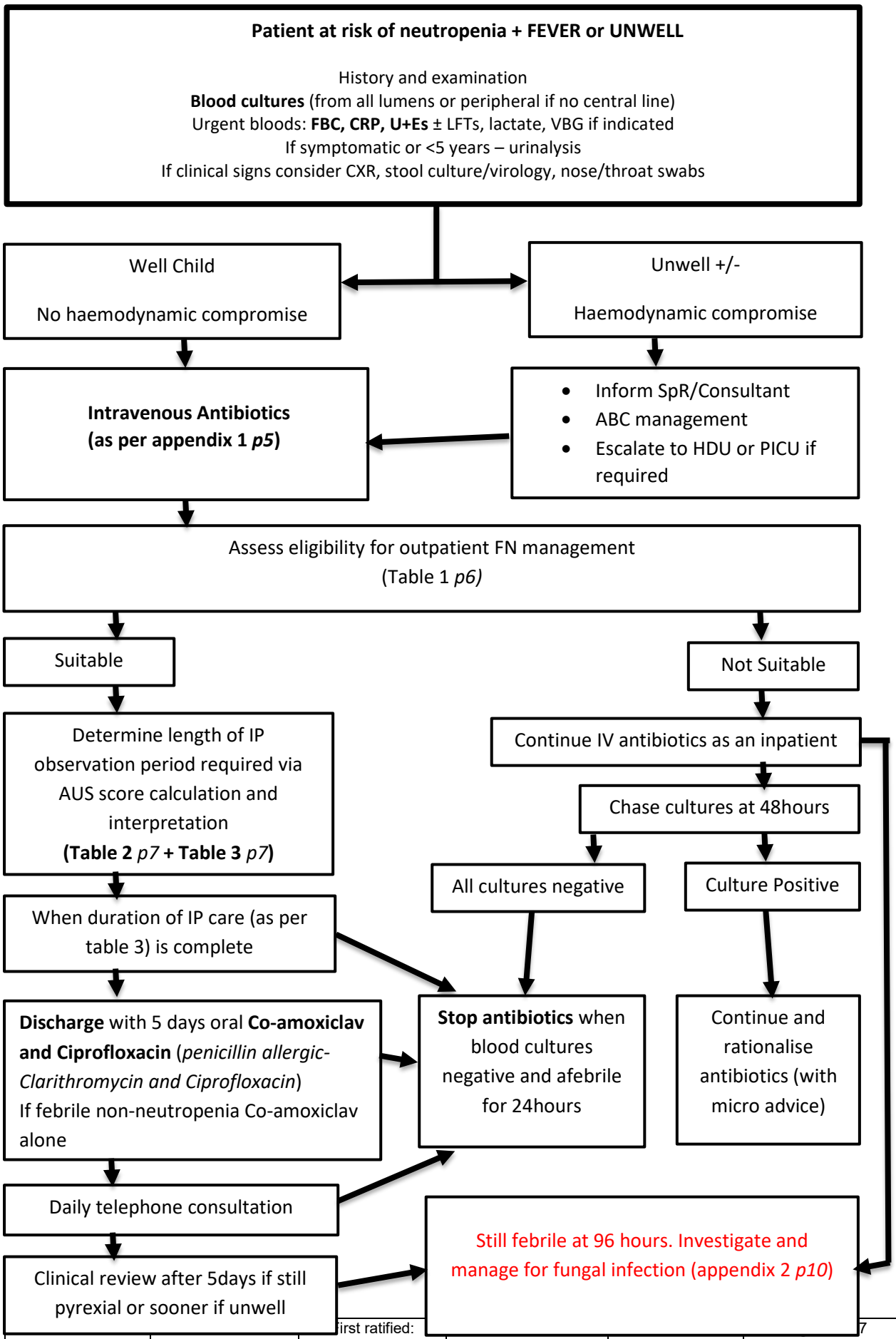
Diagnose neutropenic sepsis in patients having anticancer treatments whose:

1) Neutrophil count is 0.5 x 10^9 per litre or lower and who have either:

2) A temperature higher or equal to 38^{o}C (by any measurement) **or**

3) Other signs or symptoms consistent with clinically significant sepsis

Any oncology patient with or WITHOUT fever who has features suggestive of systemic infection should be treated with intravenous antibiotics regardless of neutrophils count


Patient at risk of neutropenia + FEVER or UNWELL
History and examination
Blood cultures (from all lumens or peripheral if no central line)
Urgent bloods: FBC, CRP, U+Es ± LFTs, lactate, VBG if indicated
If symptomatic or <5 years – urinalysis
If clinical signs consider CXR, stool culture/virology, nose/throat swabs
Well Child
No haemodynamic compromise
Unwell +/-
Haemodynamic compromise
Intravenous Antibiotics
(as per appendix 1 p5)
Inform SpR/Consultant
ABC management
Escalate to HDU or PICU if required
Assess eligibility for outpatient FN management
(Table 1 p6)
Suitable
Not Suitable
Determine length of IP observation period required via AUS score calculation and interpretation
(Table 2 p7 + Table 3 p7)
Continue IV antibiotics as an inpatient
Chase cultures at 48hours
All cultures negative
Culture Positive
When duration of IP care (as per table 3) is complete
Discharge with 5 days oral Co-amoxiclav and Ciprofloxacin (penicillin allergic- Clarithromycin and Ciprofloxacin)
If febrile non-neutropenia Co-amoxiclav alone
Stop antibiotics when blood cultures negative and afebrile for 24hours
Continue and rationalise antibiotics (with micro advice)
Daily telephone consultation
Clinical review after 5days if still pyrexial or sooner if unwell
Still febrile at 96 hours. Investigate and manage for fungal infection (appendix 2 p10)

Appendix 1: Antibiotic Choice in Febrile Neutropenia :

First Line Antibiotics Empirical

Piperacillin/tazobactam *90mg/kg IV (max 4.5g) 6 hourly*

+

Gentamicin* *7mg/kg IV once daily dosing*
(For inpatients within GOSH only, amikacin is empirical aminoglycoside due to gentamicin-resistant organisms.)

If known allergy to beta-lactams
IV or Oral **Ciprofloxacin** plus **Gentamicin** (or **amikacin**)
Consider addition of **Vancomycin/Teicoplanin** (for extra Gram-positive cover)

***Avoid Gentamicin in the following patients:**

1. **Patients who have high risk of renal impairment**: hepatoblastoma, medulloblastoma, renal tumour, Wilms tumour, high risk neuroblastoma during COJEC induction, infant ependymoma
2. **Bone tumour patients**
3. **GOSH only patient Patients who are known to have A1555G mitochondrial mutation**

Known colonization?

MRSA: Consider early addition of ***vancomycin*** after discussion with microbiology

VRE: Consider addition of ***linezolid*** after discussion with microbiology

ESBLs: Consider early use of a ***carbapenem*** at presentation of fever.

Alternative to aminoglycosides:

Oral ciprofloxacin can be used (intravenous ciprofloxacin should only be used if clinical poor gastrointestinal absorption or used to treat confirmed Gram negative central venous catheter infection).
Oral ciprofloxacin dose for children: 20mg/kg twice daily (max. per dose 750mg for severe infections)
For UCH bone tumour patients, **oral ciprofloxacin 500 mg twice a day (or 750mg twice a day** for severe infections) can be used to replace aminoglycosides

Recommendation:

1.If ***meningitis*** is suspected, use ***Meropenem*** (meningeal doses) as piperacillin / tazobactam is not appropriate and seek specialist advice from microbiology/infectious diseases

2. Continue Cotrimoxazole prophylaxis during febrile neutropenic episode

3. If patient has an ***endoprosthesis***, ***Teicoplanin must be added*** to first line antibiotics of piperacillin-tazobactam and ciprofloxacin on admission.

4. Consider adding Teicoplanin or vancomycin for penicillin allergic patients receiving ciprofloxacin and gentamicin who have significant mucositis to improve cover for Gram positive organisms.

5. Consider shunt infection in patients presenting with fever and a VP shunt in situ. These patients must be discussed promptly with the PTC and neurosurgical team. Meropenem and vancomycin would be the empirical treatment of choice if there are symptoms/signs of shunt related infection and when the other focal infections are ruled out

Patients with suspected Gram positive infection:

Vancomycin (or other agents active against aerobic Gram-positive cocci) should be considered for specific clinical indications, including:

1. Positive blood culture for Gram-positive bacteria, before final identification and susceptibility testing is available
2. Clinically suspected serious catheter-related infection (eg, chills or rigors with infusion through catheter and cellulitis around the catheter entry/exit site)
3. Skin or soft-tissue infection at any site
4. Colonization with methicillin-resistant Staphylococcus aureus
5. Haemodynamically unstable patient and suspected Gram-positive septicaemia

Table 1: Eligibility Criteria for home care:

This determines whether the patient is eligible for home care taking into account their underlying diagnosis, presenting symptoms and home circumstances.

Criteria	Yes	No
Disease status: Leukaemia/lymphoma in remission or solid tumour stable/responding		
High Risk Disease • ALL in induction • Infant ALL (except maintenance) • AML • Down's Syndrome • Any patient <12months • Aplastic anaemia • Congenital immunodeficiency • High risk neuroblastoma		
Focus of infection requiring IP care		
Severe sepsis at presentation		
Treating team prefer to manage as IP		
History of non-compliance with OP treatment		
Availability of 24hour care giver at home		
Good education of care regarding reportable symptoms		
Access to telephone		
Able to reattend within 1hour *e.g. distance and transport*		

Any highlighted RED are NOT ELIGIBLE for outpatient treatment

AUS-Score

Following the first dose of IV antibiotics **and** confirming that the patient is eligible for outpatient management (Table 1), calculate the AUS-Score (Table 2) to determine the duration of inpatient observation required (Table 3).

If there is any doubt, a patient should remain in hospital on IV antibiotics pending consultant review.

Attending or on-call consultant ought to be consulted prior to contacting the Royal Marsden Hospital for management.

Table 2: AUS-Score Calculator

AUS-rule Variables	**Yes**	**No**
Preceding chemotherapy more intensive than ALL maintenance*	1 ☐	0 ☐
Total white cell count < 0.3 x10^9/L	1 ☐	0 ☐
Platelet <50 x10^9/L (This remains valid despite including patients who may have been transfused)	1 ☐	0 ☐
TOTAL SCORE		

*All chemotherapy regimes are considered more intensive than ALL maintenance with the exceptions of:

- LCH maintenance
- Weekly vinblastine alone

Table 3: Interpretation of AUS Score

Score	Risk stratification for bacterial infection	Duration of hospital observation
0	**Very-low risk**	8 hours
1	**Low risk**	12-24 hours
2	**Moderate Risk**	24 hours
3	**High Risk**	48 hours minimum observation **AND** 24 hours minimum afebrile

All out of hours discharges should be discussed with the attending or on-call consultant. There is no formal requirement to await a ward round consultant review.

Outpatient/Home care

If eligible for home care, oral antibiotics will be provided for 5 days duration.

Oral antibiotic choice:

5 days of co-amoxiclav and ciprofloxacin (clarithromycin and ciprofloxacin in penicillin allergic patients)

If the patient is found to have Febrile Non-neutropenia they can be discharged with oral Co-amoxiclav alone. Or the advised antibiotic for the source of infection (as per Microguide/Eolas)

Daily phone calls following discharge

Following discharge, the Little Oaks/Ash ward team to call parents daily for 5 days to review the following:

*Answers marked with an Asterix below require a return to hospital for clinical review

Confirm temperature checked 4-6 hourly during day	Yes ☐ No ☐
Date and time of first fever of episode	
Ongoing fevers?	Yes ☐ No ☐ Hours of fever_____ *If >72 hours of fever – attend for review
Chills/Rigors?	**Yes*** ☐ No ☐
New fever after 24 hours afebrile?	**Yes*** ☐ No ☐
Feeling Well?	Yes ☐ **No*** ☐
Parental concern?	**Yes*** ☐ No ☐
New symptoms?	**Yes*** ☐ No ☐
Significant diarrhoea/vomiting?	**Yes*** ☐ No ☐
Severe or persistent pain?	**Yes*** ☐ No ☐
Good oral intake?	Yes ☐ **No*** ☐
Tolerating Antibiotics?	Yes ☐ **No*** ☐
Blood Culture Positive?	**Yes*** ☐ No ☐ Hours_____ Pathogen if positive:

Reasons for IP medical review

- Ongoing fever (>72 hours from presentation) or new fever after being afebrile for 24 hours
- Feeling unwell/new symptoms
- Parental concern
- Clinician concern
- Significant decrease in oral intake or significant increase in vomiting/diarrhoea
- Severe or persistent pain
- Chills/rigors
- Still febrile on day 5 of home-based care.

Reasons for re-admission

- Fever >38°C beyond 5 days from the start of the episode
- Clinically unwell
- Positive blood culture
- Infection requiring inpatient care

Reasons for discontinuing antibiotics

- Afebrile for >24hours
- Clinically well
- Blood cultures negative at 48hours.

Appendix 2:

Ongoing management after 96 hours intravenous antibiotic treatment if persistent fever:

1. All patients who are febrile and neutropenic at 96 hours should be discussed with the PTC.
2. Only consider switching antibiotics if clinical deterioration or microbiological indication i.e. positive blood culture
3. Consider fungal infection especially in high risk patient

Fungal Investigations:

- **Early chest HR-CT**
- **Abdo US**
- **Serum Galactomannan, B Glucan**

Investigations to consider: (for patients with probable or proven pulmonary fungal infection, even when neurologically asymptomatic).

- **MRI or CT brain with contrast**

Treatment: (Empirical antifungal use):

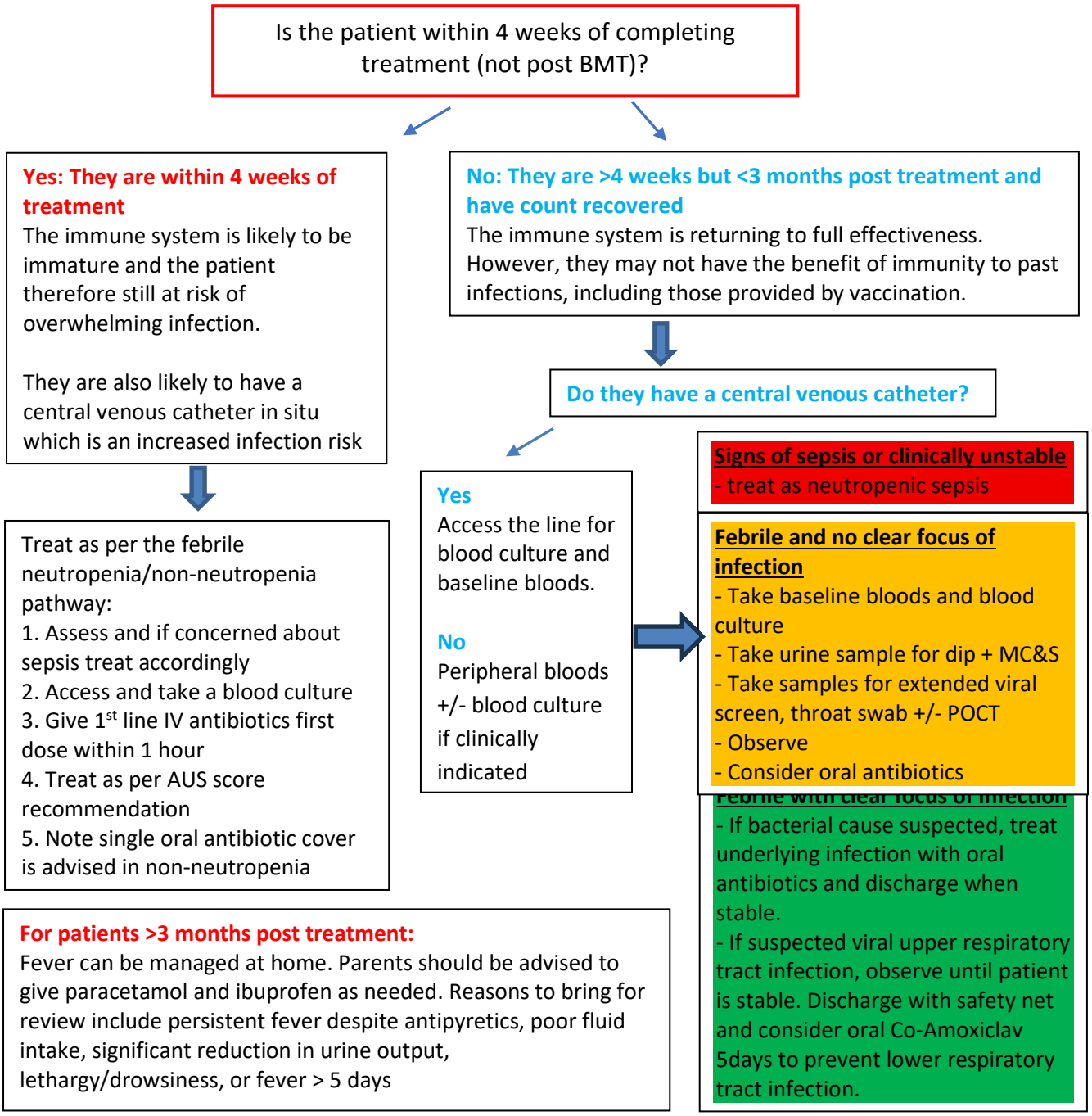
- **Liposomal amphotericin B (Ambisome) 3 mg/kg once a day.**
- **Consider Caspofungin following discussion with oncology team**

Management of fever in children following completion of chemotherapy treatment

This guidance is not to be used for those post stem cell transplant

The Children & Young People's Cancer Association (CCLG) have completed a systematic review of available research with the aim of answering how best to manage fever in children who have completed cancer treatment, but the data was limited and no conclusion was drawn. The CCLG is now conducting an international meta-analysis.

In the meantime, please follow this general guidance which is based on experience and common sense.



2. Supporting References

Supportive Care Protocol version Dec 2020

CCLG febrile neutropenia pathway

Clinical Practice Guideline for systematic antifungal prophylaxis in paediatric patients with cancer and HSCT recipients. Journal of Clinical Oncology

Febrile Neutropenia or Suspected Bacterial Infection: Initial Management – Guideline- Sheffield's Children's NHS Foundations Trust (Updated on 24 January 2024)

3. Supporting relevant trust guidelines

2. Guideline Governance

a. Scope

This guideline is relevant to all staff caring for all children from 0-18 years old across the emergency department, inpatient ward and outpatient department.

b. Purpose

i. This guidelines aims to facilitate a common approach to the management of children. At times deviation from the guideline may be necessary, this should be documented and is the responsibility of the attending consultant.

ii. This guideline is subject to regular review to ensure ongoing evidence based practice.

c. Duties and Responsibilities

All healthcare professionals responsible for the care of all children 0-18years should be aware of practice according to this guideline.

d. Approval and Ratification

This guideline will be approved and ratified by the Paediatric Guidelines Group.

e. Dissemination and Implementation

i. This guideline will be uploaded to the trust intranet 'Paediatric Guidelines' page and thus available for common use.
ii. This guideline will be shared as part of ongoing education within the Paediatric Department for both medical and nursing staff.
iii. All members of staff are invited to attend and give comments on the guideline as part of the ratification process.

f. Review and Revision Arrangements

a. This policy will be reviewed on a 3 yearly basis by the appropriate persons.
b. If new information comes to light prior to the review date, an earlier review will be prompted.
c. Amendments to the document shall be clearly marked on the document control sheet and the updated version uploaded to the intranet. Minor amendments will be ratified through the Paediatric Guidelines Group. A minor amendment would consist of no major change in process, and includes but is not limited to, amendments to documents within the appendices.

g. Equality Impact Assessment

Background • Who was involved in the Equality Impact Assessment
Author and the supervising consultants.
Methodology • A brief account of how the likely effects of the policy was assessed (to include race and ethnic origin, disability, gender, culture, religion or belief, sexual orientation, age) • The data sources and any other information used • The consultation that was carried out (who, why and how?)
All groups of staff and patients were taken into consideration and there is no bias towards or against any particular group.
Key Findings • Describe the results of the assessment • Identify if there is adverse or a potentially adverse impacts for any equalities groups
There is no evidence of discrimination.
Conclusion • Provide a summary of the overall conclusions
There is no evidence of discrimination.
Recommendations • State recommended changes to the proposed policy as a result of the impact assessment • Where it has not been possible to amend the policy, provide the detail of any actions that have been identified • Describe the plans for reviewing the assessment
This guideline is appropriate for use.

h. Document Checklist

To be completed (electronically) and attached to any document which guides practice when submitted to the appropriate committee for approval or ratification.

Title of the document: Febrile Neutropenia and Non-neutropenia in Paediatric Oncology Patients

Policy (document) Author: Dr Claire Mitchell

Executive Director: N/A

		Yes/No/ Unsure/NA	Comments
1.	**Title**		
	Is the title clear and unambiguous?	**Y**	
	Is it clear whether the document is a guideline, policy, protocol or standard?	**Y**	
2.	**Scope/Purpose**		
	Is the target population clear and unambiguous?	**Y**	
	Is the purpose of the document clear?	**Y**	
	Are the intended outcomes described?	**Y**	
	Are the statements clear and unambiguous?	**Y**	
3.	**Development Process**		
	Is there evidence of engagement with stakeholders and users?	**N**	
	Who was engaged in a review of the document (list committees/ individuals)?		**Oncology team**
	Has the policy template been followed (i.e. is the format correct)?	**Y**	
4.	**Evidence Base**		

		Yes/No/ Unsure/NA	Comments
	Is the type of evidence to support the document identified explicitly?	**Y**	**Taken from CCLG Low Risk Febrile Neutropenia pathway, and Supportive Care Protocol v5**
	Are local/organisational supporting documents referenced?	**Y**	
5.	**Approval**		
	Does the document identify which committee/group will approve/ratify it?	**Y**	**Paediatric Guideline Committee**
	If appropriate, have the joint human resources/staff side committee (or equivalent) approved the document?	**N/A**	
6.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	**Y**	
	Does the plan include the necessary training/support to ensure compliance?	**Y**	
7.	**Process for Monitoring Compliance**		
	Are there measurable standards or KPIs to support monitoring compliance of the document?	**N**	
8.	**Review Date**		
	Is the review date identified and is this acceptable?	**Y**	
9.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for coordinating the dissemination, implementation and review of the documentation?	**Y**	

		Yes/No/ Unsure/NA	Comments
10.	**Equality Impact Assessment (EIA)**		
	Has a suitable EIA been completed?	Y	

Committee Approval (Paediatric Guidelines Group)			
If the committee is happy to approve this document, please complete the section below, date it and return it to the Policy (document) Owner			
Name of Chair	**Alexandra Jones**	**Date**	**13th November 2024**
Ratification by Management Executive (if appropriate)			
If the Management Executive is happy to ratify this document, please complete the date of ratification below and advise the Policy (document) Owner			
Date:			