

AMBULATORY PATHWAY FOR ONCOLOGY PATIENTS PRESENTING WITH LOW RISK FEBRILE NEUTROPENIA

Acute Oncology Neutropenia Working Party

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- This document is offered as a template for use by trusts/hospitals wishing to develop a pathway for the ambulatory management of patients with low risk febrile neutropenia.
 - Trusts/hospitals should review content and amend/adapt if required to suit local services prior to approval for local use.
 - The user organisation must accept governance responsibility for implementation of the pathway.

Disclaimer

The information contained in this guideline is a consensus of the development and consultation groups' views on current treatment.

It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance process. Care has been taken in the preparation of the information contained in the guideline.

Nevertheless, any person seeking to consult the guideline, apply its recommendations or use its content is expected to use independent, personal medical and/or clinical judgment in the context of the individual clinical circumstances, or to seek out the supervision of a qualified clinician. The group makes no representation or guarantee of any kind whatsoever regarding the guidelines content or its use or application and disclaim any responsibility for its use or application in any way.

1.0 Introduction

Outpatient management of patients with low risk febrile neutropenia (LRFN) identified by a validated risk stratification tool e.g. Multinational Association of Supportive Care in Cancer (MASCC) score <https://www.mascc.org/mascc-fn-risk-index-score> and/or Clinical Index of Stable Febrile Neutropenia (CISNE) <https://www.mdcalc.com/clinical-index-stable-febrile-neutropenia-cisne> is a safe and effective strategy.

The benefits include admission avoidance, reducing pressure on often overcrowded and overstretched emergency departments, cost savings, reduced risk of nosocomial infections as well as improved patient experience and satisfaction ^{1,2,3,4,5}

The National Institute for Health and Care Excellence guideline CG151 recommends considering outpatient antibiotic therapy for patients with confirmed neutropenic sepsis and a low risk of developing septic complications, taking into account the patient's social and clinical circumstances and discussing with them the need to return to hospital promptly if a problem develops⁶.

This document is a template for use by trusts/hospitals wishing to develop a pathway for the ambulatory management of patients with a low risk febrile neutropenia of undefined source. It is not intended for use in the management of LRFN in patients who are receiving treatment for Haematological Malignancy.

For governance purposes trusts/hospitals should review and approve the content for local use and amend/adapt if required to suit local services.

2.0 Clinical Workup

Fever in a neutropenic patient is an acute medical emergency.

There is no clinically defined temperature threshold to guide antibiotic prescribing in suspected febrile neutropenia and clinical judgement is required at all times. Patients, receiving systemic anti-cancer therapy (SACT) who contact oncology 24- hour advice lines, or present to the acute setting with a temperature of 37.5⁰C or above or 36.0⁰C or below, or who are generally unwell, irrespective of fever, should proceed to urgent clinical assessment as recommended in current UKONS 24-hour triage guidance⁷.

Assessment should include:

- A thorough history taken, and examination performed
- We recommend referring to NHSE guidance and the use of NEWS 2 ⁸ <https://www.england.nhs.uk/wp-content/uploads/2017/09/sepsis-guidance-implementation-advice-for-adults.pdf>
- Patients with low risk febrile neutropenia will not trigger an aggregate NEWS score of 5 and may not trigger a single NEWS parameter of 3. However, recent chemotherapy is a **red flag** on the UK Sepsis Trust Pathway – clinicians should commence Sepsis 6 whilst awaiting blood results and completing MASCC risk assessment.

<https://sepsistrust.org/wp-content/uploads/2018/06/Inpatient-adult-NICE-Final-1107-2-1.pdf>

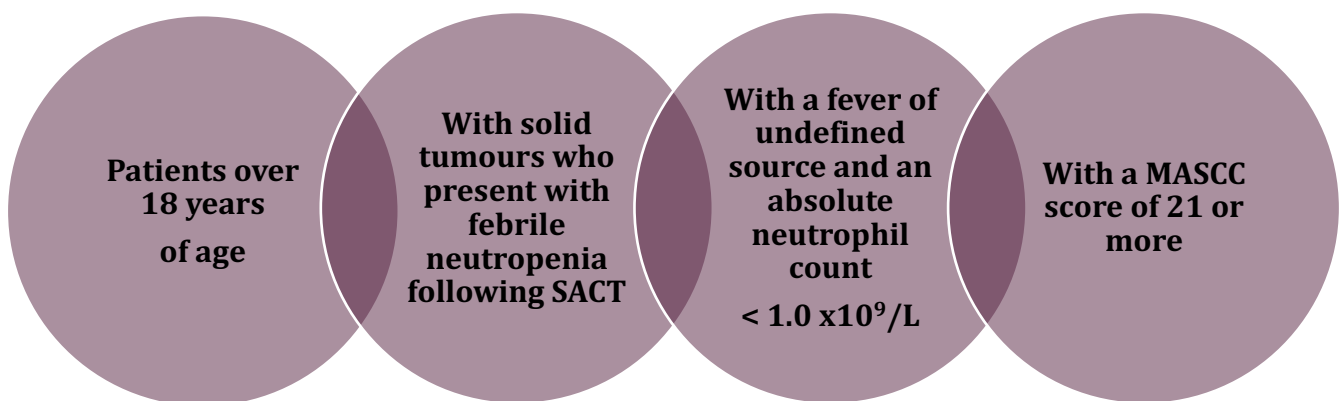
- Take blood for full blood count, urea and electrolytes, liver function tests (including serum albumin), C-reactive protein and lactate along with peripheral blood cultures. Blood cultures should also be taken from any central venous access devices present. A chest x-ray should be performed and/or other specimens, such as MSU sent for culture and sensitivity testing if clinically indicated. Urinalysis may also be helpful. Consider viral illness e.g., influenza and take required swabs. Isolate the patient whilst in the department if indicated
- First dose of empirical intravenous antibiotic therapy administered within 1 hour in all patients where sepsis is suspected
- If Neutropenia confirmed (absolute neutrophil count $< 1.0 \times 10^9/L$)⁹ complete MASCC assessment (p.8)

3.0 Defining Patients with Low Risk Febrile Neutropenia

Patients with febrile neutropenia are a heterogeneous group with only a minority of treated patients developing significant medical complications. Once initial workup is performed, a MASCC score should be calculated (p.8). Patients with a MASCC score of 21 or more are at low risk for complications and **may** be suitable for ambulatory outpatient management. A period of observation is advised to assess and confirm clinical stability, although evidence-based guidance is limited, ASCO/IDSA suggest a period of 4 hours^{9,10,12}

4.0 Low Risk Pathway Inclusion Criteria

Fig 1. Primary Inclusion Criteria



4.1 Secondary criteria for inclusion in the low risk pathway:

- History of a temperature of 37.5°C or above or 36.0°C or below ⁷
- First dose of empirical intravenous antibiotic therapy administered
- The patient has ready access to an Emergency Department
- The patient is able to tolerate oral therapy, and there are no other contraindications to commencing oral therapy

N.B. Patients with an identified specific focus of infection should be managed according to local microbiological protocols.

5.0 Clinical Management for Ambulatory Low Risk Febrile Neutropenia

- It is important to consider local sensitivity and resistance patterns in determining the most appropriate regimen, so be guided by local microbiological guidelines.
- If not contraindicated by local/regional guidance, commence oral antimicrobial therapy with oral amoxicillin/clavulanic acid (500/125mg TDS) and ciprofloxacin (500mg BD) subject to local microbiology guidance. If penicillin allergic or known fluoroquinolone resistance, seek local microbiology guidance.
- The duration of oral antibiotics should be determined locally with scope for ongoing review according to clinical response and microbiological culture results
- Advise the patient to complete any prophylactic G-CSF prescribed with their chemotherapy regimen but do not start G-CSF ^{6,9,11,12}
- Provide additional support treatment as indicated
- Inform the acute oncology team and/or the oncology treating team of assessment and entry onto low risk ambulatory pathway to ensure;
 - clinical follow up and assessment according to agreed LRFN local practice
 - the oncology treating team are aware of this complication and can manage further SACT accordingly

6.0 Requirements to Manage Patients in An Ambulatory Setting

- The patient does not have any of the following conditions that may preclude them from entering onto the low risk pathway:
 - Reduced cognitive function
 - Language barriers
 - Mental health problems
 - Learning difficulties

- The patient understands the signs and symptoms that should trigger them to seek medical assessment and knows when they should return to the hospital (see patient information leaflet on page.12). Check the patients understanding of the instructions given and their understanding of the potential risks of not following the advice/instructions
- The patient has a telephone and is able to access the 24-hour specialist oncology advice line
- The patient has access to a carer and support in the community
- The patient has transport available should they need to return
- The patient has ready access to an Emergency Department
- The patient has an appointment for review by telephone or in an ambulatory setting as per agreed hospital protocol. We recommend review within 48 hours.
- Blood test (FBC) request form completed and given to the patient with instruction for use, if appropriate

7.0 Clinical Follow Up

- Review the patient by telephone or in an ambulatory setting to assess clinical progress, we recommend that this initial review takes place within 48 hours, further review should be planned according to clinical assessment and progress.
- The assessment should include at least the following key actions:
 - Repeat and review the full blood count if appropriate
 - Review results of cultures that were taken on initial assessment
 - Consider rationalising antimicrobials
 - Inform patient's treating Oncology team

All patients contacting/presenting with a temperature of 37.5°C or above or 36.0°C or below or generally unwell post SACT, should proceed to urgent clinical assessment as per UKONS 24 Hour Triage guidance ⁶. They should have:

- A thorough history taken, examination performed, and observations recorded and reviewed
- Completion of NEWS2 <https://www.england.nhs.uk/wp-content/uploads/2017/09/sepsis-guidance-implementation-advice-for-adults.pdf> ⁸ and the Sepsis Trust Inpatient Screening and Action Tool - <https://sepsistrust.org/wp-content/uploads/2018/06/Inpatient-adult-NICE-Final-1107-2-1.pdf> **If sepsis Red Flags present, then proceed to Sepsis Six management pathway - NB Recent chemotherapy is a Red Flag.**
- Take blood for full blood count, urea and electrolytes, liver function tests (including serum albumin), C-reactive protein and lactate along with peripheral blood cultures. Blood cultures should also be taken from any central venous access devices present. A chest x-ray should be performed and/or other specimens such as MSU, sent for culture and sensitivity testing if clinically indicated. Urinalysis may be helpful. Consider viral illness e.g., influenza and take required swabs.
- Isolate the patient whilst in the department if indicated.
- First dose of empirical intravenous antibiotic therapy administered within 1 hour in all patients where sepsis is suspected.

• **Once initial workup is complete, a MASCC score should be calculated (P.8)**

MASCC Score of **21 or more** - complete ambulatory low risk febrile neutropenia pathway checklist:

- Patient is over 18yrs old
- Patient has a solid tumour
- History of a temperature of 37.5°C or above or 36.0°C or below ⁷
- Patient has received systemic anti-cancer therapy
- Patient has an absolute neutrophil count <1.0 x 10⁹/L
- First dose of empirical intravenous antibiotic therapy administered
- The patient has ready access to an Emergency Department

The patient should be observed for an agreed minimum period of time to ensure clinical stability. We recommend a minimum of 4 hours ^{9,10,12}.

* If patient remains stable

* If the patient's condition worsens

MASCC Score **below 21**

Inpatient management of neutropenic sepsis

**Patient's condition worsens
Re-assess NEWS2 and Sepsis Red flags**

- Commence oral antimicrobial therapy with amoxicillin/clavulanic acid (500/125mg TDS) and ciprofloxacin (500mg BD) It is important to consider local sensitivity and resistance patterns in determining the most appropriate regimen so be guided by local microbiological guidelines. If penicillin allergic or known fluoroquinolone resistance, seek local microbiology guidance. The duration of oral antibiotics should be determined locally with scope for ongoing review according to clinical response and microbiological culture results
- Advise the patient to complete any prophylactic G-CSF previously prescribed but do not start G-CSF ^{6,9,11,12}
- Provide additional support treatment as indicated

- Update the Acute Oncology team of assessment and entry onto low risk ambulatory pathway to ensure appropriate follow up and management. (N.B. local reporting/communication pathway may include patient's treating oncology team)
- Ensure that the patient has an appointment for review by telephone or in an ambulatory setting as per agreed hospital protocol. We recommend review within 48 hours
- Ensure that the patient has access to 24-hour specialist oncology telephone advice line
- Ensure the patient knows the signs and symptoms that should trigger them to seek medical assessment and know when they should return to the hospital

- Review the patient by telephone or in an ambulatory setting to assess clinical progress. We recommend review within 48 hours:
 - Repeat and review the full blood count if appropriate
 - Review results of cultures that were taken on initial assessment
 - Consider rationalising antimicrobials
 - Inform patient's treating oncology team
 - Further review should be planned according to clinical assessment and patient progress.

8.1 – Multinational Association for Supportive Care in Cancer Risk Score.
(MASCC <https://www.mascc.org/mascc-fn-risk-index-score>)

Patient identification details/label		Hospital and department:		
		Date and time of arrival: Date..... Time.....		
MASCC Risk Index Scoring system		Yes	No	Score
Burden of illness (febrile neutropenia) (Select only one of these 3 options, points are not cumulative)	No or mild symptoms	5	0	
	Moderate symptoms	3	0	
	Severe symptoms or moribund	0	0	
Is the systolic blood pressure < 90mmHg?		0	5	
Does the patient have chronic obstructive pulmonary disease?		0	4	
Does the patient have a solid tumour		4	0	
Is the patient dehydrated requiring IV fluids?		0	3	
Did the patient develop febrile neutropenia while an outpatient?		3	0	
Is the patient < 60 years old?		2	0	
Total MASCC Score				
Maximum theoretical score is 26 MASCC score of 21 or more are considered at low risk of septic complications				

Assessment record - MASCC completed by:	
Name:	Designation:
Signature:	Date:

8.2 Ambulatory Low Risk Febrile Neutropenia Pathway Checklist

1. Inclusion criteria :	✓yes × no
Patient is over 18 years of age	
Patient has a solid tumour	
A history a temperature of 37.5°C or above or 36.0°C or below	
Has received systemic anti-cancer treatment	
An absolute neutrophil count <1.0 x 10 ⁹ /L	
Please record neutrophil count here = X10 ⁹ /L	
First dose of empirical intravenous antibiotic therapy administered	
MASCC score of 21 or more	
If YES to all the above proceed to the action checklist:	
2.Action checklist :	✓ yes × no
History, examination and observations complete	
The following blood tests performed and reviewed:	
Full Blood Count	
Urea and electrolytes	
Liver function tests (including serum albumin)	
C-reactive protein	
Lactate	
All blood results above are within acceptable parameters	
Blood samples taken for culture	
MASCC Score calculated =	
If blood results are clinically acceptable and the patients MASCC score is 21 or above proceed to ambulatory discharge checklist:	
3. Ambulatory discharge checklist	✓ yes × no
Confirm clinical and patient agreement to proceed to discharge	
The patient has access to a carer and support in the community	

Patient verbalises: 1. That they understand the risk of sepsis and that it is a life-threatening condition. 2. They know the signs and symptoms that should alert them to seek medical assessment and are prepared to call and return to the hospital if needed	
Patient has ready access to an Emergency Department	
Patient written information (see P.12) and emergency contact details including for the 24-hour oncology telephone advice line number provided	
The patient has a thermometer and knows how and when to measure their temperature	
Confirm that the patient is able to tolerate, and there is no contraindication to oral therapy. Oral antimicrobial therapy prescribed and dispensed	
Blood test (FBC) request form completed and given to the patient with instruction for use, if appropriate	
Appointment for review by telephone or in an ambulatory setting as per hospital protocol. We recommend review within 48 hours	
Local Acute Oncology team/patient's Oncology team updated, and clinical follow up arrangements confirmed	
If YES to all of the above: proceed to discharge and ambulatory management.	

Practitioner record Checklists 1,2 and 3 completed by:			
Name:	Designation:	Signature:	Date

4. Clinical follow up checklist :	✓ yes ✗ no
Patient reviewed by telephone or in an ambulatory setting to ensure the patient making good clinical progress.	
Repeat the full blood count if appropriate and review the result	
Review results of cultures that were taken on initial assessment.	
If neutrophils have recovered and cultures negative, consider rationalising antimicrobials	
Update patient's treating Oncology team.	
Further review should be planned according to clinical assessment and patient progress	

Practitioner record Clinical Follow up checklist completed by:			
Name:	Designation:	Signature:	Date

6. Supplementary notes:

Practitioner supplementary notes:

Name:

Designation:

Signature:

Date:

N.B. Please retain a copy of this document for the patients record. Information can be supplemented by freehand text in the notes box above.

Information for patients who have a low white blood cell count and an infection following chemotherapy that can be managed as an outpatient.

You have developed an infection and also currently have a low white blood cell count as a result of your chemotherapy treatment.

Your healthcare team have examined you and performed various blood tests, they feel it is safe to discharge you home with antibiotic tablet treatment for your infection.

We know this is safe practice and of benefit to patients.

However, patients occasionally need to return to hospital and have antibiotics intravenously through a drip.

There is a risk that your infection could develop into sepsis (blood poisoning), which can be a life-threatening complication, so we ask you to be vigilant and contact the **24-hour advice line immediately** if you experience any of the following:

- You feel worse
- You are not improving despite taking the antibiotic tablets as instructed
- You have new or worsening symptoms e.g.
 - Feeling generally unwell, not able to get out of bed. Flu like symptoms - feeling cold and shivery, headaches, aching muscles
 - Change in temperature – 37.5°C or higher OR below 36°C
 - Coughing up green phlegm
 - A sore throat
 - Diarrhoea - 4 or more loose, watery bowel movements in 24 hours
 - Being sick/vomiting
 - Pain or burning when passing urine
 - Skin changes – redness, hotness, swelling or pain
 - Redness, pain, hotness or swelling around your central line if you have one.

After discharge:

- You have been given a follow up review appointment. It is very important that this review takes place, so that we are able to monitor your progress and make changes to treatment if required.
- You have been given antibiotic tablets; please take these regularly as directed. Contact the 24-hour advice line if you have any problems in taking the tablets as directed.
- **24 Hour Advice Line Number:**

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The UK Chemotherapy Board – representation includes:

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Royal College of Pathologists (**RCPATH**).
United Kingdom Oncology Nursing Society (**UKONS**)
British Oncology Pharmacy Association (**BOPA**)

References:

1. Klastersky J, Paesmans M. *The Multinational Association for Supportive Care in Cancer (MASCC) risk score: 10 years of use for identifying low risk neutropenic cancer patients. Support Care Cancer* 2013; 21: 1487-95
2. Teuffel O, Ethier M, Alibhal S et al. *Outpatient management of cancer patients with febrile neutropenia: a systematic review and meta-analysis. Ann Oncol* 2011; 22: 2358-65
3. Vidal L, Ben dor I, Paul M et al; *Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients. Cochrane systematic Review. Oct 2013*
4. Rivas-Ruiz R, Villasis-Keever V, Miranda-Novales G et al; *Outpatient treatment for people with cancer who develop low risk febrile neutropenic fever. Cochrane Systematic Review review of OPD low March 19*
5. Taplitz RA. *Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America Clinical Practice Guideline Update. J Clin Oncol* 36: 1443-1453 2018
6. NICE. *Neutropenic sepsis: prevention and management in people with cancer. Clinical guideline [CG151] Published date: 19 September 2012*
7. UKONS. *Oncology/Haematology 24 Hour triage tool (2016) <https://www.ukons.org>*
8. NHSE. *Sepsis guidance implementation advice for adults (2017) <https://www.england.nhs.uk/wp-content/uploads/2017/09/sepsis-guidance-implementation-advice-for-adults.pdf>*
9. ASCO: *Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: <http://ascopubs.org/doi/10.1200/JCO.2017.77.6211>*
10. Kern WV, Marchetti O, Drgona L et al. *Oral antibiotics for fever in low-risk neutropenic patients with cancer: a double-blind, multicenter trial comparing single daily moxifloxacin with twice daily ciprofloxacin plus amoxicillin-clavulanic acid combination therapy – EORTC infectious diseases group trial XV. J Clin Oncol* 2013; 31: 1149–1156.
11. Smith TJ, Bohlke K, Lyman GH et al; *Recommendations for the use of white blood cell growth factors: American Society of Clinical Oncology Clinical Practice Guideline update 2015)*
12. IDSA *Clinical Practice Guidelines: Clinical Infectious Diseases, Volume 52, Issue 4, 15 February 2011, Pages e56–e93*