



Medical management of Neutropenic Sepsis / Febrile Neutropenia in adult Oncology / Haematology patients Procedure

1. Guiding Principles

Effective: 1 November 2021

Febrile Neutropenia (Neutropenic fever) is defined as¹:

Temperature of 38°C or greater and neutrophil count of less than 0.5×10^9 cells/L, or less than 1.0×10^9 cells/L and predicted to fall to lower than 0.5×10^9 cells/L.

Neutropenic patients are at risk of developing severe, life-threatening infection.

All febrile patients receiving chemotherapy should be presumed to be neutropenic until proven otherwise.

Neutropenic sepsis, with or without fever, is a medical emergency. All clinical signs indicating sepsis need to be acted on immediately and management of febrile neutropenia commenced.

The elderly or those on steroids may not become febrile, despite neutropenic sepsis.

The administration of empiric antibiotics is not to be delayed awaiting confirmation of blood culture results or absolute neutrophil count for patients at risk of neutropenia with a fever or signs of infection.

'Neutropenic precautions' refer to additional nursing and general care practices that can be put in place to reduce this risk to inpatient, neutropenic patients. Neutropenic precautions are required when the total white cell count is $<1 \times 10^9$ and/or neutrophil count $< 1 \times 10^9$

WA Country Health Service (WACHS) has endorse the [Electronic Therapeutic Guidelines \(eTG\)](#) as the primary reference.

2. Procedure

Neutropenic sepsis, with or without fever, is a medical emergency.

- Aim to start intravenous antibiotics as soon as febrile neutropenia is suspected in a patient, delay of more than 1 hour is associated with inferior outcomes.
- For a ward-based patient developing febrile neutropenia - if there are signs of sepsis or septic shock - **start antibiotics within 30 minutes** (refer to [eTG Principles of managing sepsis and septic shock: Early recognition in adults](#) for definitions in adults).

Do NOT wait for the FBP before starting antibiotics. Any delay in the commencement of antibiotics may cause increased morbidity and mortality.

3. Definitions

Neutropenia	An absolute decrease in the number of circulating neutrophils to less than $1.0 \times 10^9/L$.
Febrile neutropenia¹	Temperature of at least $38.3^\circ C$ (or at least $38^\circ C$ on two occasions) and neutrophil count of less than 0.5×10^9 cells/L, or less than 1.0×10^9 cells/L and predicted to fall to lower than 0.5×10^9 cells/L, or if such a patient is systemically unwell with a clinical suspicion of sepsis.

4. Roles and Responsibilities

4.1 Admitting Doctor

Initial Management

Step 1

- Resuscitation / stabilisation of patient, as required.
- Consider oxygen and intravenous fluids.

Step 2

- Perform septic workup. **Do not wait for results.** Optimally obtain blood cultures first, but **do not delay** the commencement of antibiotics:
 - Blood cultures
 - if no central venous catheter (CVC): two sets (aerobic and anaerobic bottles) from separate peripheral sites
 - if CVC: 1 set from each lumen of CVC and one set from peripheral blood
 - Full blood count
 - Urea and electrolyte
 - Liver function test
 - Mid-Stream Urine / Catheter Specimen Urine
 - Sputum (if clinically indicated)
 - Faeces (if clinically indicated)
 - Swab of CVC exit site (if clinically indicated)
 - Swab of any other suspicious wounds/focal lesions (if clinically indicated)
 - Make arrangements for chest x-ray.

Step 3

- Commence empiric intravenous antibiotic therapy as soon as febrile neutropenia is suspected.
- **Delay of more than 1 hour** is associated with inferior outcomes. **Do not wait** for the FBP before starting antibiotics.
- This is initial therapy only and subsequent treatment remains at the discretion of the treating clinician.

The doses below apply to adults with normal renal function. If the patient has known renal impairment, refer to [Appendix A](#) for appropriate dose adjustments. Treatment should not be delayed to ascertain kidney function if this is not already known.

- **First line therapy** (ensure patient is not penicillin allergic)
 - Piperacillin / Tazobactam 4g / 500mg IV 6 hourly
 - **Non life-threatening penicillin allergy** (e.g. rash)
 - Cefepime 2g IV 8 hourly
 - **Life threatening penicillin / beta lactam allergy:**
 - Vancomycin 25-30mg/kg (loading dose) (If CrCL >90mL / min) or 1g IV if CrCL 60-90mL / min) then switch to weight -based maintenance dosing
- PLUS**
- Ciprofloxacin 400mg IV 12 hourly.

If patient has systemic compromise (e.g. hypotension, hypoxia, organ dysfunction), **add the following** to piperacillin/tazobactam:

- Vancomycin 25-30mg/kg (loading dose) (If CrCL >90ml / min) or 1g IV 12 hourly if CrCL 60-90ml / min) switch to weight- based maintenance dosing

AND

- Gentamicin 4-7mg/kg 24 hourly (ideal body weight)

Refer to: WACHS [Specialised Medication- Intravenous Vancomycin in Adults Guideline](#) for the weight based loading dose and maintenance dose tables

If further deterioration change Piperacillin/tazobactam to Meropenem, cease gentamicin, continue Vancomycin, and discuss with Infectious Disease Specialist:

- Meropenem 1g IV 8 hourly
- Vancomycin 25-30mg/kg (loading dose) (If CrCL >90ml / min) or
- 1g IV 12 hourly if CrCL 60-90ml / min)

Consult with Infectious Disease Specialist early.

Special considerations:

- If the patient is colonised with a multi-resistant organism, he/she is at risk of developing an infection with the same organism. **In this case, early discussion with an infectious disease specialist is recommended.**
- If patient has obvious cellulitis / CVC infection / is colonized with MRSA and has skin breakdown, add vancomycin.
- If patient has features of abdominal or perineal infection, metronidazole 500mg IV 12 hourly may be required when using cefepime.
- If not improving, consider further investigations including HRCT sinuses/chest and serum galactomannan.
- If any indication of possible fungal infection or if patient is on prophylactic antifungal therapy, consider adding:
 - Anidulafungin 100mg IV 24-hourly.

Step 4

- **Escalation of care: Early discussion with an infectious disease specialist is recommended.**
- Ensure Consultant Physician, or their registrar, is phoned to review the patient (via switch), and the chemotherapy unit is aware of admission (9892 2494).
- If unavailable, the Oncology on call consultant from Fiona Stanley Hospital can be contacted for advice. Seek a consultant opinion about the use of granulocyte colony stimulating factor (filgrastim or pegylated filgrastim – see Step 9).
- Assess likelihood of complications and document this in the notes.
- Low risk of complications:
 - Appears well.
 - Systolic blood pressure (BP) greater than 100mmHg, or blood pressure same as patient's usual BP.
 - No dyspnoea / hypoxia.
 - Eating and drinking well.
 - No signs of focal infection.
- High risk of complications:
 - Systolic BP less than or equal to 90 mmHg, or 30 mmHg below patient's usual BP, or patient requiring vasopressor support.
 - Room air PaO₂ less than or equal to 60 mmHg, or O₂ saturation less than or equal to 90%, or requirement for mechanical ventilation.
 - Confusion or altered mental state.
 - Disseminated intravascular coagulation, or new abnormal PT / APTT.
 - New organ failure.
 - New cardiac arrhythmia.

Step 5

- Arrange admission, as care is to be as an inpatient for a minimum of 24 – 48 hours, or longer depending on assessment of risk of complications. A single room, labelled as 'neutropenic precautions' is required.
- Refer to the following procedures for the nursing and additional infection control precautions required on the ward:
 - WACHS Great Southern [Infection Control Link Nurse Role and Responsibilities - Procedure -Albany Hospital](#)
 - WACHS [Nursing Management of the Neutropenic ADULT Haematology and Oncology Patient Procedure](#)

Ongoing Management

Step 6

- Follow up any positive culture results. Modification of the initial empiric antibiotics may be required.
- Avoid paracetamol unless significant symptoms from fever as it may mask ongoing temperature spikes and make following treatment response more difficult.

Step 7

- Decide on **duration of IV antibiotic** therapy
 - Low risk patients with solid malignancies are to receive IV antibiotics for 48 hours prior to considering change to oral antibiotics (e.g. Amoxicillin/clavulanate)

+ ciprofloxacin if no penicillin allergy; clindamycin + ciprofloxacin if penicillin allergy; single agent amoxicillin/clavulanate if fluoroquinolone allergy).

Step 8

- Decide on **total duration of antibiotic** therapy
 - If patient continues to be low risk, and becomes afebrile within 3 – 5 days, but still has a neutrophil count less than $0.5 \times 10^9 / L$, continue antibiotics for minimum of 7 days.
 - If fever recurs while neutropenic and on oral antibiotics, IV therapy is to be reinstated.
 - If patient has become afebrile and neutrophil count now greater than $0.5 \times 10^9 / L$, antibiotic therapy can be ceased.

Step 9

- Consider the use of **Granulocyte Colony Stimulating Factor**
 - This would be a decision made in consultation with a physician or oncologist.
 - Choice of granulocyte colony stimulating factor
 - If the patient fits the PBS Criteria and the patient is an outpatient or day patient, then Pegfilgrastim is to be used as a single dose (unlikely as patient will usually be admitted).
 - If the patient does not fit the PBS Criteria and/or is an inpatient, then filgrastim (daily dosing) is to be used.

4.2 All Staff

All staff are required to work within policies and guidelines to make sure that WACHS is a safe, equitable and positive place to be.

5. Compliance

Failure to comply with this procedure may constitute a breach of the WA Health Code of Conduct (Code). The Code is part of the [Integrity Policy Framework](#) issued pursuant to section 26 of the [Health Services Act 2016](#) (WA) and is binding on all WACHS staff which for this purpose includes trainees, students, volunteers, researchers, contractors for service (including all visiting health professionals and agency staff) and persons delivering training or education within WACHS.

WACHS staff are reminded that compliance with all policies is mandatory.

6. Records Management

All WACHS clinical records must be managed in accordance with [Health Record Management Policy](#).

7. Evaluation

Monitoring of compliance with this document is to be carried out by the Great Southern Rural Cancer Nurse and the Medical Registrar, every admission using the following means / tools:

- Audit of compliance with guidelines using designed audit tool and presented quarterly at the Cancer Leadership Meeting.

8. Standards

[National Safety and Quality Health Service Standards: 4, 8](#)

9. Legislation

Nil

10. References

1. [Cancer Institute NSW eviQ Standard Cancer Treatments](#) – Immediate management of neutropenic fever.
2. Australian Consensus Guidelines for the management of neutropenic fever in adult cancer patients. Internal Medicine Journal 2011; 41 (Suppl 1)
3. [Inpatient Management of the Neutropenic Patient – Procedure – Albany Hospital](#)

11. Related Forms

Nil

12. Related Policy Documents

WACHS [Nursing Management of the Neutropenic ADULT Haematology and Oncology Patient Procedure](#)

WACHS [Specialised Medication - Intravenous Vancomycin in Adults Guideline](#)

WACHS [Infection Control Link Nurse Role and Responsibilities - Procedure - Albany Hospital](#)

WACHS [Inpatient Management of the Neutropenic Patient – Procedure – Albany Hospital](#)

13. Related WA Health System Policies

Nil

14. Policy Framework

[Clinical Governance, Safety and Quality](#)

15. Appendix

Appendix A: [Renal impairment dosing table](#)

**This document can be made available in alternative formats
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Contact:	Consultant Medical Oncologist		
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Version:	5.00	Date Published:	1 November 2021

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Appendix A: Renal impairment dosing table

Piperacillin/tazobactam	CL _{CR} < 20mL/min	100% 12-hourly
Cefepime	CL _{CR} 10-50mL/min	50 to 100% 12- to 24-hourly
	CL _{CR} < 10mL/min	25 to 50% 24-hourly
Ciprofloxacin	CL _{CR} 10-30mL/min	50% 12-hourly or 100% 24-hourly
	CL _{CR} < 10mL/min	100% 24-hourly
Meropenem	CL _{CR} 10-25mL/min	50% 8 to 12-hourly
	CL _{CR} < 10mL/min	50-100% 24-hourly
Anidulafungin	100mg 24-hourly (no adjustment needed)	

Table 1: Antimicrobial dosage adjustment in renal impairment