SA Health

Febrile Neutropenia Management (Adults) Clinical Guideline

Version 2.0

Approval date: 18 October 2023

Government of South Australia
SA Health

Disclaimer

This state-wide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion, with consideration to antibiotic resistance epidemiology in South Australia. In facilities where the prevalence of multi-resistant organisms may differ, local hospital guidelines may take precedence. Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation. If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom and detailed reasons for the departure from the guideline.

This state-wide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for:

- Discussing care with consumers in an environment that is culturally appropriate, and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advising consumers of their choice and ensure informed consent is obtained
- Providing care within scope of practice, meeting all legislative requirements, and maintaining standards of professional conduct
- Documenting all care in accordance with mandatory and local requirements.

Information in this state-wide guideline is current at the time of publication. SA Health does not accept responsibility for the quality or accuracy of material on websites linked from this site and does not sponsor, approve, or endorse materials on such links.

Contents

1. Definitions and acronyms

AGEP	Acute generalised exanthematous pustulosis
CVC	Central venous catheter
DRESS	Drug reaction with eosinophilia and systemic symptoms
Empiric treatment	Treatment initiated prior to a confirmed diagnosis and microbiology laboratory finding
Febrile	Having or showing the symptoms of a fever (≥ 38°C)
Febrile neutropenia emergency letter	A referral letter providing instruction for emergency departments regarding prompt assessment and treatment of patients at risk (see Appendix 7)
ICU	Intensive care unit
IV	Intravenous
MBA20	Multiple biochemical analyses – 20 tests
MC&S	Microscopy, culture, and sensitivity
MDR	Multidrug-resistant
MRSA	Methicillin resistant *Staphylococcus aureus*
NAT	Nucleic acid test
Neutropenia	The presence of abnormally few neutrophils in the blood, leading to increased susceptibility to infection (neutrophils < 1.0 x 10^9/L)
PCR	Polymerase chain reaction
PICC	Peripherally inserted central catheter
SAAGAR	South Australian expert Advisory Group on Antimicrobial Resistance
SBP	Systolic blood pressure
SJS	Stevens-Johnson syndrome
TEN	Toxic epidermal necrolysis

2. Introduction

This guideline has been developed by the South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR) to guide clinicians towards best practice in the initial management of febrile neutropenia in adult patients.

The aim of this guideline is to assist clinicians to:

- Determine probable febrile neutropenia
- Stabilise the patient
- Order the relevant investigations
- Consider the need for intensive care unit (ICU) consultation or transfer to a tertiary centre
- Prescribe appropriate initial antibiotic therapy

Ongoing therapy and duration of therapy should be determined by the patient's response, isolation of a pathogen, and rate of neutrophil recovery.

Key stewardship points

- Administer IV antibiotics within 30 minutes of presentation for greatest survival benefit.
- Obtain blood cultures ***before*** commencing antibiotics but do not delay if there is difficult access.
- If available, review recent microbiology for positive cultures to guide antibiotic choice to cover previous isolates.
- Monotherapy with an anti-pseudomonal beta-lactam antibiotic is the recommended first line empiric treatment in clinically stable patients with no signs of sepsis or septic shock.
- Adjust treatment as soon as additional information is available (e.g., source of infection, results of Gram stain, culture, or susceptibility testing), or there is no improvement after 48 hours.
- Duration of antibiotic therapy is dependent on response to antibiotic therapy, rate of neutrophil recovery, and resolution of infection.

3. Background and aetiology

Febrile neutropenia is a medical emergency requiring rapid assessment and prompt initiation of antibiotics. Delays in the initiation of antibiotics can lead to high morbidity and high mortality.

Febrile neutropenia is most often seen in patients with cancer receiving cytotoxic antineoplastic therapy. It may also be a complication in patients who have had a stem cell or bone marrow transplant, or who are immunosuppressed on disease modifying therapy. All patients presenting with fever (≥ 38°C) following chemotherapy should be managed as if they have febrile neutropenia and receive empiric treatment without waiting for laboratory confirmation of neutrophil count.[1]

Often, fever is the only sign of infection as the levels of neutrophils are not enough to launch a significant inflammatory response. Neutropenic patients can present without a fever, especially if the patient is elderly or taking corticosteroids.[2]

The range of pathogens that are implicated in febrile neutropenia is vast with most cases caused by the patient's endogenous flora.

Although an uncommon cause of febrile neutropenia, *Pseudomonas* is linked to a high risk of morbidity and mortality. Therefore, empiric treatment with broad spectrum anti-pseudomonal cover is needed. Gram-

positive cocci such as *Staphylococcus epidermis* and *Staphylococcus aureus* are the most common cause of febrile neutropenia. Despite this, vancomycin is not recommended for routine empiric treatment as no additional benefits have been seen in controlled trials.[3]

4. Investigations

Where possible, aerobic and anaerobic blood samples for culture should be taken prior to administering antibiotics. However, antibiotic administration should not be delayed in cases of difficult access. Two sets of samples (i.e., four bottles) should be collected from separate sites (e.g., a peripheral site and the access device (for patients with a central venous access device)).

See ***Appendix 1: Pathway / protocol*** for information regarding further investigations.

5. Antibiotic choice

Monotherapy with an anti-pseudomonal beta-lactam antibiotic is the recommended first line therapy for the empiric treatment of febrile neutropenia unless there is a documented high-risk beta-lactam allergy. Piperacillin/tazobactam is an appropriate choice in patients with no documented penicillin allergy, whilst cefepime is recommended in patients with a moderate risk penicillin allergy. In high-risk beta-lactam allergy, ciprofloxacin may be used. However, given that it has inadequate Gram-positive coverage, ciprofloxacin should be combined with vancomycin when used as empiric therapy.

In patients with severe sepsis or septic shock, the addition of gentamicin for multidrug-resistant (MDR) Gram-negative bacteria, and vancomycin for methicillin resistant *Staphylococcus aureus* (MRSA) cover, is recommended.

In all patients with febrile neutropenia who have features of abdominal or perineal infection, consider adding metronidazole to the cefepime and ciprofloxacin/vancomycin empiric regimens. Metronidazole is not necessary if the patient is receiving piperacillin/tazobactam, as piperacillin/tazobactam provides adequate anaerobic cover.

The routine addition of vancomycin to empiric treatment is not usually recommended in the clinically stable patient with no features of sepsis. There is evidence to show that it does not reduce mortality and is associated with an increased risk of adverse events.[4,5] However, consider adding vancomycin in those patients known or suspected to be colonised with MRSA, with skin/soft tissue/catheter-related infections, or in severe sepsis or septic shock (as outlined above).

If there is no evidence of positive cultures for resistant organisms, empiric vancomycin should be ceased after 48-72 hours, and empiric gentamicin should be ceased after 24-48 hours.

Review clinical and microbiological status at 24-48 hours and change to directed therapy if a pathogen is identified with susceptibilities in the blood culture.

Refer to ***Appendix 1: Pathway / protocol*** for further information on antibiotic choice.

6. Duration of therapy

Cessation of antibiotics or step-down to oral therapy may be considered when there has been resolution of neutropenia (i.e., if neutrophil count has recovered to at least 0.5 x 10^9/L) and

- the patient has become afebrile within 3-5 days of commencing antibiotic therapy,
- no causative organism is isolated, and
- no other clinical syndrome is present.

If neutrophil count is less than 0.5 x 10^9/L and neutropenia is expected to be prolonged, cessation of antibiotics should be based on the clinical judgement of the individual clinician. Cessation of antibiotics may be considered if the mucous membranes and integument are intact, and there is no impending invasive procedure or ablative chemotherapy planned.[1]

7. Penicillin / cephalosporin hypersensitivity

Penicillin allergy is often misdiagnosed and there is increasing evidence that patients with an inaccurate allergy 'label' receive higher rates of broad-spectrum antibiotics.[6] Alternative antibiotic recommendations are included in this guideline for patients with moderate risk penicillin allergy (e.g., delayed rash which is not urticarial or DRESS / SJS / TEN / AGEP). This guideline also includes recommendations for patients with high-risk penicillin or cephalosporin allergy (e.g., anaphylaxis, urticaria, angioedema, bronchospasm, DRESS / SJS / TEN / AGEP), however, it is recommended that expert advice should still be sought from an infectious diseases / clinical microbiology specialist.

For more information on the classification of penicillin and cephalosporin allergies, see ***Appendix 5: Assessment of patients who report hypersensitivity to penicillins***, and refer to the Penicillin and Cephalosporin Allergies webpage on the SA Health website.[7]

8. Febrile neutropenia emergency letter

Patients who have received anti-neoplastic agents (chemotherapy) or have been deemed to be at high risk of developing febrile neutropenia should be provided with a febrile neutropenia emergency letter (see ***Appendix 6: Template for Febrile Neutropenia Emergency Letter***).

The patient should be advised to present this letter to treating clinicians when unwell to ensure they are triaged appropriately, and treatment is provided within the timeframes specified in this guideline.

9. Safety, quality and risk management

National Safety and Quality Health Service Standards

 Clinical Governance	 Partnering with Consumers	 Preventing and Controlling Infections	 Medication Safety	 Comprehensive Care	 Communicating for Safety	 Blood Management	 Recognising and Responding to Acute Deterioration
☐	☐	☒	☒	☐	☐	☐	☐

The following actions of the relevant standards are applicable:

Standard 3 – Preventing and Controlling Infections

- Actions 3.18, 3.19: Antimicrobial stewardship – The health service organisation has systems for the safe and appropriate prescribing and use of antimicrobials as part of an antimicrobial stewardship program.

Standard 4 – Medication Safety

- Action 4.01: Integrating clinical governance – Clinicians use the safety and quality systems from the Clinical Governance Standard when implementing policies and procedures for medication management, managing risks associated with medication management, and identifying training requirements for medication management.

10. Principles of the standard

National standard 3, *Preventing and Controlling Infections,* aims to reduce the risk to patients, consumers, and members of the workforce of acquiring preventable infections; effectively manage infections, if they occur; prevent and contain antimicrobial resistance; promote appropriate prescribing and use of antimicrobials as part of antimicrobial stewardship; and promote appropriate and sustainable use of infection prevention and control resources.

National standard 4, *Medication Safety,* aims to ensure clinicians are competent to safely prescribe, dispense and administer appropriate medicines and to monitor medicine use. To ensure consumers are informed about medicines and understand their individual medicine needs and risk.

11. References

1 Tam, C. S. *et al.* Use of empiric antimicrobial therapy in neutropenic fever. *Internal Medicine Journal* **41b**, 90-101 (2011).

2 Antibiotic Expert Groups. Therapeutic Guidelines: Antibiotic (online). (Melbourne, 2021).

3 Beyar-Katz, O. *et al.* Empirical antibiotics targeting gram-positive bacteria for the treatment of febrile neutropenic patients with cancer *Cochrane Database of Systematic Reviews*, Art No. CD003914 (2017).

4 Paul, M., Borok, S., Fraser, A., Vidal, L. & Leibovici, L. Empirical antibiotics against Gram-positive infections for febrile neutropenia: systematic review and meta-analysis of randomized controlled trials. *Journal of Antimicrobial Chemotherapy* **55**, 436-444 (2005).

5 Vardakas, K. Z., Samonis, G., Chrysanthopoulou, S. A., Bliziotis, I. A. & Falagas, M. E. Role of glycopeptides as part of initial empirical treatment of febrile neutropenic patients: a meta-analysis of randomised controlled trials. *The Lancet infectious diseases* **5**, 431-439 (2005).

6 Chen, J. & Khan, D. Evaluation of penicillin allergy in the hospitalized patient: Opportunities for antimicrobial stewardship *Curr Allergy Asthma Rep* **17**, 40 (2017).

7 *Penicillin and cephalosporin allergies*, <https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+programs+and+practice+guidelines/medicines+and+drugs/antibiotic+allergies/penicillin+and+cephalosporin+allergies > (Accessed July 2023).

8 Amoah, J., Klein, E. Y., Chiotos, K., Cosgrove, S. E. & Tamma, P. D. Administration of a β-lactam prior to vancomycin as the first dose of antibiotic therapy improves survival in patients with bloodstream infections. *Clinical Infectious Diseases* **75**, 98-104 (2022).

9 *Vancomycin Dosing and Monitoring in Adults Clinical Guideline*, <https://www.sahealth.sa.gov.au/wps/wcm/connect/28a702e2-eca3-47ac-bcab-4d620cc20808/Vancomycin_dosing_monitoring_guideline_v1.1_Final_Approved+Oct+2020+update.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-28a702e2-eca3-47ac-bcab-4d620cc20808-ojFXC2y > (Accessed July 2023).

10 *Aminoglycosides: Recommendations for use, dosing and monitoring Clinical Guideline*, <https://www.sahealth.sa.gov.au/wps/wcm/connect/e4c8cb004877c5c3a295f67675638bd8/Aminoglycosides_Recommendations_for_use_dosing_and_monitoring_Clinical_Guideline_v3_11.12.2020.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-e4c8cb004877c5c3a295f67675638bd8-oxOeS49 > (Accessed July 2023).
11 Reardon, J., Lau, T. T. Y. & Ensom, M. H. H. Vancomycin Loading Doses: A Systematic Review. *Ann. Pharmacother.* **49**, 557-565 (2015).
12 Winter, M. A., Guhr, K. N. & Berg, G. M. Impact of Various Body Weights and Serum Creatinine Concentrations on the Bias and Accuracy of the C ockcroft-G ault Equation. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* **32**, 604-612 (2012).
13 Gilbert, D., Chambers, H., Saag, M. & Pavia, A. (2020).

12. Document Ownership

Developed by: The South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR)
Contact: HealthAntibio@sa.gov.au
Endorsed by: Domain Custodian, Clinical Governance, Safety and Quality
Next review due: 31/08/2026
ISBN number:
CGSQ reference:
CPG history: Is this a new clinical guideline (V1)? **N**
Does this clinical guideline amend or update an existing clinical guideline? **Y**
If so, which version? **V1.0**
Does this clinical guideline replace another clinical guideline with a different title? **N**
If so, which clinical guideline (title)?
Contact for enquiries: HealthAntibio@sa.gov.au

13. Document History

Version	Date approved	Approved by	Amendment notes
2	18/10/2023	Domain Custodian, Clinical Governance, Safety and Quality	Updated to new Clinical Guideline template
1	10/10/2017	Safety & Quality Strategic Governance Committee	Original approved

14. Appendices

14.1 Appendix 1: Pathway / protocol

Initial management and treatment guideline for patients presenting to the Emergency Department with suspected febrile neutropenia

Presentation

Consider febrile neutropenia in a patient if they have a recorded temperature ≥ 38°C (or are not febrile but shows signs of shock – consider sepsis without fever) **AND**:

- Have had a stem cell or bone marrow transplant within the last 3 months, **OR**
- Have been prescribed long term steroids for Graft vs. Host Disease, **OR**
- Present with a 'Febrile Neutropenia Emergency Letter' (see Appendix 6), **OR**
- Have had recent chemotherapy, e.g., in the last 4 weeks, **OR**
- Are known to be neutropenic: neutrophils < 1.0 x 10^9/L.

FOR GREATEST SURVIVAL BENEFIT, ADMINISTER IV ANTIBIOTICS WITHIN 30 MINUTES. DO NOT WAIT FOR BLOOD RESULTS.

Note: signs of infection may be subtle or absent as neutropenic patients may exhibit little or no inflammatory response.

Does the patient show signs of shock?
(e.g., hypotension, tachypnoea, hypoxaemia, organ dysfunction, confusion, raised serum lactate)

Yes

Stabilise patient

- ☐ Urgent review by medical officer / resus team immediately (within a maximum of 30 minutes) (see Box A)
- ☐ IV access, fluid resuscitation, urgent bloods taken
- ☐ Commence empiric antibiotic therapy within 30 minutes
- ☐ Commence fluid balance chart and 15-minute observations
- ☐ Consider ICU admission or urgent MedSTAR retrieval (see Box B)

No

Does the patient have a 'Febrile Neutropenia Emergency Letter'?

Yes

Follow instructions in Febrile Neutropenia Emergency Letter

No

1. Complete urgent investigations (see Box A) **AND**
2. Commence empiric antibiotic therapy **within 30 minutes**

Box A: Investigations

Urgent – complete immediately:

Septic screen:

- ☐ Aerobic and anaerobic blood cultures from peripheral vein and CVC / PICC (if present) prior to antibiotics **IF ABLE**, but do not delay antibiotics
- ☐ Lactate (if available)
- ☐ Sputum and urine specimen for MC&S
- ☐ Complete blood count
- ☐ MBA20
- ☐ CRP

Non-urgent – complete within 1-2 hours, as clinically indicated:

- ☐ Chest x-ray or CT chest if respiratory infection likely
- ☐ Respiratory viral PCR if clinically indicated
- ☐ If diarrhoea present, stool sample for NAT panel and *C. difficile* PCR
- ☐ Other swabs (for culture / viral PCR) as clinically indicated, e.g., mouth, wounds, or lesion(s)
- ☐ Consider blood sterile site PCR, CMV viral load, cryptococcal Ag according to patient risk

Box B: Considerations for ICU admission or urgent MedSTAR retrieval (MedSTAR contact number: 13 78 27)

- Not responding to resuscitation
- Altered conscious state
- Hypoxia not corrected by oxygen therapy
- Lactate remains > 2mmol/L despite intervention
- Clinical deterioration in any other form

Empiric antibiotic therapy for febrile neutropenia

Prior to commencing empiric antibiotics, review recent microbiology for previous positive cultures. The antibiotic regimen should be chosen to ensure coverage of previous isolates. For patients colonised, or recently infected with a multidrug-resistant pathogen (e.g., ESBL-producing bacterium), consultation with ID/Micro is recommended.

Note: Doses provided are for patients with normal renal function. See Appendix 4 for dose adjustments in renal impairment. For further information on penicillin / cephalosporin allergies, see Appendix 5.

For greatest survival benefit, administer IV antibiotics within 30 minutes
NOTE: Administration of beta-lactams before vancomycin has been shown to improve survival[8]

No penicillin or cephalosporin allergy	**Piperacillin / tazobactam 4.5g IV 6-hourly**
Moderate risk penicillin allergy (e.g., delayed rash which is NOT urticarial or DRESS/SJS/TEN/AGEP)	**Cefepime 2g IV 8-hourly**
High risk penicillin or cephalosporin allergy (e.g., anaphylaxis, angioedema, bronchospasm, urticaria, DRESS/SJS/TEN/AGEP)	**Ciprofloxacin 400mg IV 12-hourly** **PLUS** **Vancomycin 25mg/kg IV (actual body weight) (max dose 3g) for initial dose** (see Appendix 2) then refer to the state-wide Vancomycin Dosing and Monitoring Clinical Practice Guideline[9] for subsequent dosing *If allergic to vancomycin contact ID/Micro for advice*
PLUS for patients with:	- Severe sepsis or septic shock, SBP <90mmHg or lactate >2mmol/L, **OR** - Onset of sepsis 48 hours after admission to hospital, **OR** - Previous resistant Gram-negative isolates **ADD** **Gentamicin IV 7mg/kg (CrCl >60ml/min) or 5mg/kg (CrCl <60ml/min) (ideal body weight¥) for initial dose** then refer to state-wide Aminoglycosides: Recommendations for Use, Dosing and Monitoring[10] guideline if subsequent dosing required *Prompt antibiotic initiation is essential, do not delay gentamicin administration to ascertain kidney function* Empiric gentamicin should not continue beyond 48 hours
PLUS for patients with:	- Severe sepsis or septic shock, or skin/soft tissue/catheter-related infection, or clinical deterioration (whilst receiving first line beta-lactam therapy), **OR** - Is known or suspected to be colonised with MRSA, **OR** - Is not responding to first line beta-lactam therapy with central venous access PLUS culture negative PLUS low index of suspicion for fungal infection **ADD (if not already prescribed above)** **Vancomycin 25mg/kg IV (actual body weight) (max dose 3g) for initial dose** (see Appendix 2) then refer to the state-wide Vancomycin Dosing and Monitoring Clinical Practice Guideline[9] for subsequent dosing Cease empiric vancomycin after 72 hours if no evidence of Gram-positive infection *If allergic to vancomycin contact ID/Micro for advice*
PLUS for patients with:	Features of intra-abdominal infection, e.g., diverticulitis/typhlitis or perineal abscess/collection **ADD** **Metronidazole 500mg IV 12-hourly** (only add to cefepime or ciprofloxacin/vancomycin regimens^)

Review therapy if culture positive or no improvement after 48 hours

^Metronidazole is not necessary if the patient is receiving piperacillin/tazobactam, as piperacillin/tazobactam provides adequate anaerobic cover.

¥Use actual body weight (ABW) if less than patient's ideal body weight (IBW). For obese patients (BMI 30-34kg/m^2) use adjusted body weight (AdjBW), for BMI ≥ 35kg/m^2, seek expert advice.

14.2 Appendix 2: Vancomycin loading dose

Based on the currently available evidence, clinical data support a loading dose of **25mg/kg (actual body weight).**[2] A loading dose may facilitate more rapid attainment of therapeutic target range.[2,11]

Table 1: Vancomycin loading dose

Actual body weight (kg)	Loading dose (grams)
40-44	1g
45-54	1.25g
55-64	1.5g
65-79	2g
80-119 **OR** ≥ 120kg and GFR < 59ml/min	2.5g
≥ 120kg and GFR ≥ 60ml/min	3g (maximum dose)

For subsequent doses refer to the state-wide Vancomycin Dosing and Monitoring Clinical Practice Guideline.[9]

14.3 Appendix 3: Calculating creatinine clearance

Ideal body weight estimation chart [2]

Height		Ideal body weight (kg)	
Cm	Feet & inches	Female	Male
155	5'1	48	53
160	5'3	53	57
165	5'5	57	62
170	5'7	62	66
175	5'9	66	71
180	5'11	71	75
185	6'1	75	80
190	6'3	80	84
195	6'4	84	89
200	6'6	89	93

IBW (female) = 45.5kg + 0.9kg per cm over 152cm

IBW (male) = 50kg + 0.9kg per cm over 152cm

Cockcroft-Gault equation for estimating creatinine clearance

$$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{IBW (kg)}^{\wedge} \times 0.85 \text{ (for females)}}{0.815 \times \text{SeCr (micromol/L)}}$$

^ Use actual body weight (ABW) if this is less than ideal body weight (IBW)

^ **If obese** (BMI ≥ 30 kg/m^2) consider using adjusted body weight (AdjBW) to calculate creatinine clearance [12]:

AdjBW = IBW + 0.4 x (ABW - IBW)

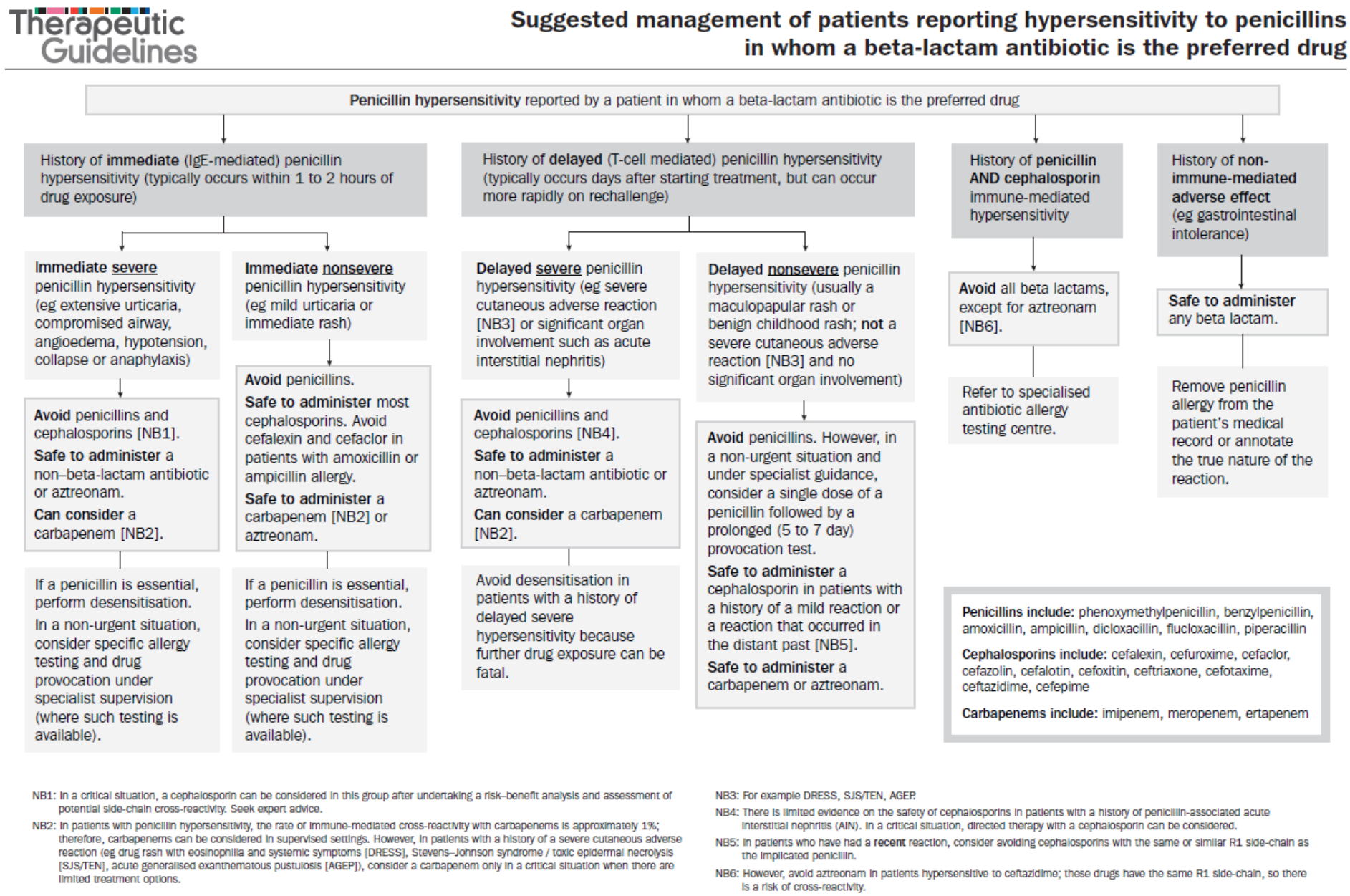
Note: Cautions when using Cockcroft-Gault equation:

- Muscle wasting – CrCl will be overestimated
- Acute renal failure – CrCl may represent non-steady state serum creatinine levels and may underestimate the level of renal impairment
- Elderly – CrCl can overestimate renal function in the elderly

14.4 Appendix 4: Medication dose adjustment recommendations in renal impairment [2,13]

Drug	Dose adjustment in renal impairment
Cefepime IV	*CrCl 30-60ml/min:* 2g IV 12-hourly *CrCl 11-29ml/min:* 2g IV 24-hourly *CrCl <11ml/min:* 1g IV 24-hourly
Ciprofloxacin IV	*CrCl 31-50ml/min:* 400mg IV 12-hourly *CrCl 10-30ml/min:* 200mg IV 12-hourly **OR** 400mg IV 24-hourly *CrCl <10ml/min*: 400mg IV 24-hourly
Gentamicin IV – single dose Use IBW or ABW, whichever is less. For obese patients (BMI 30-34kg/m^2) use AdjBW – see Appendix 3. For BMI ≥35 kg/m^2, seek expert advice. Refer to the Aminoglycosides: Recommendations for Use, Dosing and Monitoring Clinical Guideline[10] if further dosing is required.	*CrCl 40-60ml/min:* 5mg/kg IV *CrCl <40ml/min:* 4mg/kg IV
Piperacillin / tazobactam IV	*CrCl 20-40ml/min:* 4.5g IV 8-hourly *CrCl <20ml/min:* 4.5g IV 12-hourly
For dosing in dialysis patients, refer to the *Therapeutic Guidelines: Antimicrobial dosages for adults with impaired renal function.*	

14.5 Appendix 5: Assessment of patients who report hypersensitivity to penicillins



14.6 Appendix 6: Template for Febrile Neutropenia Emergency Letter

Medical Emergency Triage Letter – Risk of Febrile Neutropenia

Treating team: Haematology/Oncology/other (circle)	
Treating consultant contact details:	
Diagnosis:	Date:

Attach patient details sticker before giving this letter to your patient

Allergies:

Additional clinical information:
Provide any additional relevant clinical information for this patient, including colonised or recent infection with multidrug-resistant organisms

Dear doctor / triage nurse,

This patient is currently receiving _____chemotherapy and has a high risk of developing febrile neutropenia. If the patient has either a recorded temperature greater than or equal to 38°C, **or** is afebrile but feeling unwell, **they are likely to be profoundly neutropenic – at least priority 2 triage:**

- Take blood cultures **before** starting antibiotics (but do not delay giving antibiotics).
- **Administer empiric antibiotic therapy within 30 minutes of presentation** (see below) for greatest survival benefit. Do not wait for blood results.
- Review recent microbiology for positive culture if readily available to guide antibiotic choice to cover previous pathogens (do not delay antibiotic administration if this information is not readily available).

Investigations:

Urgent (complete immediately):

- ☐ Aerobic and anaerobic blood cultures from peripheral vein and CVC / PICC (if present), *prior to antibiotics* **IF ABLE**, but do not delay antibiotics
- ☐ Sputum and urine specimen for MC&S
- ☐ Complete blood count
- ☐ MBA20
- ☐ Lactate (if available)
- ☐ CRP
- ☐ Secure IV access / fluid resuscitation

Within 1-2 hours of presentation:

- ☐ Chest x-ray or CT chest if respiratory infection likely
- ☐ Respiratory viral PCR if clinically indicated
- ☐ Other swabs (for culture / viral PCR) as clinically indicated, e.g., mouth, wounds, or lesion(s)
- ☐ If diarrhoea present, stool sample for NAT panel and *C. difficile* PCR
- ☐ Consider blood sterile site PCR, CMV viral load, cryptococcal Ag according to patient risk
- ☐ Notify Haematology / Oncology registrar during working hours or on-call registrar / RMO after hours

Empiric antibiotic therapy for febrile neutropenia

Initial therapy will need to be reviewed once results of investigations and blood cultures are available

Note: Doses provided below are for patients with normal renal function. See Appendix 4 for dose adjustments in renal impairment.

No penicillin or cephalosporin allergy	**Piperacillin / tazobactam 4.5g IV 6-hourly**
Moderate risk penicillin allergy (e.g., delayed rash which is NOT urticarial or DRESS/SJS/TEN/AGEP)	**Cefepime 2g IV 8-hourly**
High risk penicillin or cephalosporin allergy (e.g., anaphylaxis, angioedema, bronchospasm, urticaria, DRESS/SJS/TEN/AGEP)	**Ciprofloxacin 400mg IV 12-hourly** **PLUS** **Vancomycin 25mg/kg IV (actual body weight) (max dose 3g) for initial dose** (see Appendix 2) then refer to the state-wide Vancomycin Dosing and Monitoring Clinical Practice Guideline for subsequent dosing *If allergic to vancomycin contact ID/Micro for advice*
PLUS for patients with:	- Severe sepsis or septic shock, SBP <90mmHg or lactate >2mmol/L, **OR** - Onset of sepsis 48 hours after admission to hospital, **OR** - Previous resistant Gram-negative isolates **ADD** **Gentamicin IV 7mg/kg (CrCl >60ml/min) or 5mg/kg (CrCl <60ml/min) (ideal body weight^) for initial dose** then refer to state-wide Aminoglycosides: Recommendations for Use, Dosing and Monitoring guideline if subsequent dosing required *Prompt antibiotic initiation is essential, do not delay gentamicin administration to ascertain kidney function* Empiric gentamicin should not continue beyond 48 hours
PLUS for patients with:	- Severe sepsis or septic shock, or skin/soft tissue/catheter-related infection, or clinical deterioration (whilst receiving first line beta-lactam therapy), **OR** - Is known or suspected to be colonised with MRSA, **OR** - Is not responding to first line beta-lactam therapy with central venous access PLUS culture negative PLUS low index of suspicion for fungal infection **ADD (if not already prescribed above)** **Vancomycin 25mg/kg IV (actual body weight) (max dose 3g) for initial dose** (see Appendix 2) then refer to the state-wide Vancomycin Dosing and Monitoring Clinical Practice Guideline for subsequent dosing Cease empiric vancomycin after 72 hours if no evidence of Gram-positive infection *If allergic to vancomycin contact ID/Micro for advice*
PLUS for patients with:	Features of intra-abdominal infection, e.g., diverticulitis/typhlitis or perineal abscess/collection **ADD** **Metronidazole 500mg IV 12-hourly** (only add to cefepime or ciprofloxacin/vancomycin regimens^)