**Canberra Health Services**

**Guideline**

**Febrile Neutropenia Management**

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| Purpose |

This document describes the process for patients who are suspected of having febrile neutropenia within Canberra Health Services (CHS) while under the care of haematology or oncology services.

**Patient group:**

* Adult haematology and oncology patients (16 years and above) who have received antineoplastic agents recently
* For children under the age of 16 years, refer to the Guideline, *Cancer and Cancer Blood Disorders – Care of Paediatric Patients (infants, children and adolescents)* on the CHS Policy Register.

**Note:**

* All patients who are febrile post chemotherapy must be considered febrile neutropenic until proven otherwise
* This protocol can also be applied to patients who are neutropenic from other causes.

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| Alerts |

**Haematology or Oncology patients who are suspected of having febrile neutropenia require immediate attention.** Febrile Neutropenia is classified as a medical emergency. Prompt action is required. Should nursing/medical staff believe patient is critically unwell or they are worried, a Code BLUE (Medical Emergency) should be actioned**:**

* The Emergency Department is often the first point of presentation for the patient when they become ill
* Prompt medical assessment is required, as the patient can progress to severe sepsis, shock, and collapse within hours of symptoms developing (e.g. fever, rigors, evidence of line infection).
* Early administration of broad-spectrum intravenous (IV) antibiotics saves lives.

**Febrile Neutropenia:**

* Temperature greater than or equal to 380C
* Absolute Neutrophil Count (ANC) < 1x109/L

(It may be presumed that patient has neutropenia in a setting of fever and a history of chemotherapy in previous 21 days, unless proven otherwise)

**Medical review and antibiotics MUST be commenced within 30 minutes of presentation or review.**

**Note:**

Signs of infection maybe subtle or absent as neutropenic patients may exhibit little or no inflammatory response.

Consider a patient’s base line temperature when assessing fever – if a patient has a low base line temperature and is exhibiting signs of deterioration/infection but has not reached 380C, it is appropriate to assess for sepsis or febrile neutropenia (FN).

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| Scope |

This document applies to all Medical Staff, Registered Nurses, Enrolled Nurses and Pharmacists. As well as all patient care areas within CHS, and in particular, those areas where patients may first present to the health care system, including but not limited to:

* Emergency Department (ED)
* Cancer Rapid Assessment Unit (CRAU)
* Cancer Outreach Team (COT) service
* Medical Officer in the Triage Category 2 below also includes the nurse practitioner within CRAU

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| Section 1 – Emergency Department Patient Management |

* The ED or CRAU is often the first point of presentation and prompt medical assessment is required
* Early administration of broad-spectrum IV antibiotics saves lives (see Attachment 1)
* Current guidelines also recommend not delaying antibiotic administration until two sets of blood cultures are taken, especially in cases of difficult access as this can cause substantial delays
* Medical admission is required for outpatients.

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| Section 2 – Ward Priority Response to a Patient with First Episode of Febrile Neutropenia (FN) call |

For Haematology and Oncology patients, the following parameter must trigger a FN call:

* Febrile neutropenic patients (a patient who is neutropenic, ANC < 1.0X109/L and develops a temperature of 38 degrees or above [first spike]).

**NOTE:** **All patients who are febrile post chemotherapy must be considered febrile neutropenic until proven otherwise**

Please make a **FN call** to the Haematology or Medical Oncology Registrar during business hours or the after hour’s Medical Registrar (MR) and inform the nursing team leader.

The aim of this response pathway is to have a medical review of the patient and administration of antibiotics within 30 minutes of the first spike of temperature.

**First Response**

The Team or on-call Registrar must attend and review the patient within 30 minutes of a FN call being initiated. If after 30 minutes a patient was not attended, then the patient should be escalated to the on call Haematologist/Oncologist. A Code Blue/MET call must be made as per the situation.

When the primary team Registrar or the on-call MR attends or phones the ward the nurse must state the reason for the FN call and any other relevant information, and that the patient requires an urgent assessment. **The procedures outlined in this guideline are to be followed both in hours and after hours.**

The Febrile Neutropenia Response Plan must be completed. This document will ensure each step is followed in response to a patient being treated for FN.

**Second Response – The next 30 minutes after a FN call**

The initiator of the FN call must:

1. Instigate assessment
2. Collect the samples for septic screening, blood cultures and urine cultures
3. Organise CXR (may be performed by MR)
4. Initiate management as appropriate, until the MR arrives to review the patient.

Resident Medical Officers will attend FN calls to assist the registrar only. After a FN call is initiated one or more of the following four (4) outcomes may occur:

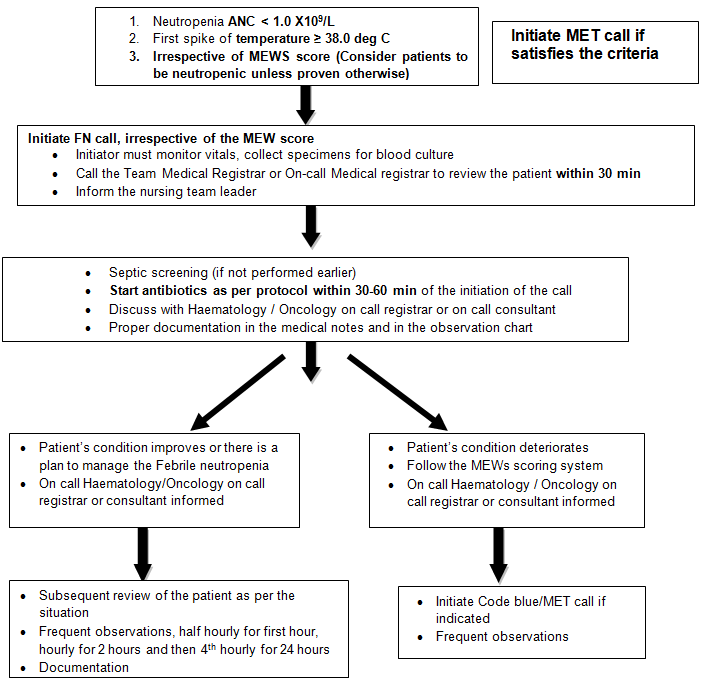
1. The patient’s condition is attended by the patient’s medical team or “on-call” MR and appropriate investigations performed, antibiotics have been commenced no further action
2. The patient’s condition deteriorates - the Code Blue/MET call must then be called
3. The decision to activate a Code Blue can be made at any point during the review and presence of the MR does not negate the need for activation if the patient has deteriorated and is meeting MET criteria
4. Thirty (30 minutes) elapses from the time of the original FN call and the team or on-call MR has either not responded, or the response is considered inadequate by the initiator or other member of nursing or medical staff:
   * Second FN call must be initiated
   * If the on-call Registrar is unavailable to review the on-call admitting consultant should be contacted
   * MET may be initiated if patient’s condition deteriorates.

**One Hour after the FN call**

After initiation of treatment the Registrar needs to monitor the patient to ensure that further deterioration is avoided and that the appropriate investigations are performed, and antibiotics has been commenced as per the departmental guideline. The frequency of observation would be as per the *Vital Signs and Early Warning Scores Procedure*, which is half hourly for the first hour, hourly for 2 hours and then 4th hourly for 24 hrs.

MET calls will continue to be made by nursing and medical staff if the patient’s clinical condition is felt as critical based on the MEWs score or otherwise and patient’s consultant should be contacted.

**Flow Chart – Management of FN in Haematology Oncology Patients (Chart 1)**



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| Section 3 – High Risk Febrile Neutropenia Patient Management |

**General Management**

1. **Assessment**

Appropriate assessment of patients as HIGH RISK for complications of febrile neutropenia is essential and is conducted by the Multinational Association for Supportive Care in Cancer (MASCC) criteria (see Section 7). If the patient at any point fulfils the criteria for MET call, please follow the relevant pathway.

*Review history:*

1. Nature and duration of antineoplastic therapy received
2. Recent history of bone marrow transplantation (date, conditioning treatment, type of transplant)
3. Vascular access (date of central line insertion, type, and site of central line)
4. Current medications, specifically recent antibiotics, filgrastim, pegfilgrastim or any granulocte stimulating factor (G-CSF).
5. Recent history of blood administration
6. Co-morbid diseases (congestive heart failure, renal impairment, chronic obstructive pulmonary disease)
7. History of allergies or adverse drug reactions
8. Prior infections
9. Recent travel, pet, gardening soil exposure.

*Initial assessment:*

1. Temperature
2. Pulse
3. Blood pressure
4. Oxygen saturation
5. Respiratory rate.

*Careful search for source of Infection:*

1. Oropharynx (including evidence of mucositis)
2. Sinuses
3. Lungs
4. Skin and nails
5. Vascular access site
6. Bone Marrow or other biopsy sites
7. Central nervous system (including signs of neck stiffness)
8. Gastrointestinal tract and abdominal examination
9. Perineum and peri-rectal area (per rectal examination is not recommended as mucosal breaks promote bacterial translocation).

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| **Note:** Signs of infection maybe subtle or absent as neutropenic patients may exhibit little or no inflammatory response. |

*Mandatory investigations required:*

1. Full Blood Count and differential (to determine neutrophil count)
2. Electrolytes, Urea, Creatinine
3. Liver Function Tests
4. C reactive protein
5. Lactate.

*Blood cultures (refer to Blood Culture Collection procedure excluding neonates on the Policy Register):*

1. 1 set peripherally
2. 1 set from each lumen of central venous access device if present
3. (2 sets peripherally if patients have no central venous access device). Note *\*Do not flush central venous access device before withdrawal of blood for blood cultures and \* Do not discard any blood (10mL drawn should be used for the cultures)*

4. Chest X-ray

5. Midstream Urine

6. Sputum Specimen (if productive cough)

7. Stool sample (for culture and *Clostridium difficile* toxin testing if diarrhoea present).

Swab of central venous catheter or any suspicious/focal lesion from previously infected sites (Note: These may begin to suppurate with the return of neutrophils and need to be managed accordingly.)

1. **Treatment protocol**

* Antibiotic therapy (IA, IB, IC, ID,)
* Ancillary treatment (IIA, IIB, IIC, IID)

Commence antibiotic treatment without waiting for blood test results.

**IA. Initial therapy**

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| **Patient group** | **Recommended Antibiotic Therapy (doses for normal renal function)** |
| **Patients without features of systemic**  **Compromise AND NO KNOWN PAST HISTORY OF ANTIMICROBIAL RESISTANT ORGANISMS\*\***  (Beta-lactam monotherapy is recommended  Unless patient hypersensitive to the recommended medicine) | **No penicillin allergy:**  gentamicin IV once daily stat according to CHS protocol\*  PLUS  piperacillin-tazobactam 4.5 g IV 6 hourly |
| **Non-life threatening penicillin allergy (rash):**  gentamicin IV once daily stat according to CHS protocol\*  PLUS  cefepime 2 g IV 8 hourly |
| **Life-threatening (immediate) penicillin allergy or**  **beta-lactam allergy:**  gentamicin IV once daily stat according to CHS protocol\*PLUS  vancomycin IV according to the Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines follow links to the antibiotic, febrile neutropenia section |
| **Patients with systemic compromise** | meropenem 1 g IV eight hourly  PLUS  vancomycin IV according to Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines site follow links to the antibiotic, febrile neutropenia section |
| **Patients with obviously**  **infected vascular devices, or MRSA carriers with extensive skin breaks / desquamation** | As for ***patients without features of systemic compromise***  PLUS  vancomycin IV according to Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines site follow links to the antibiotic, febrile neutropenia section. |
| **Patients with features of abdominal or**  **perineal infection AND NO KNOWN PAST HISTORY OF ANTIMICROBIAL RESISTANT ORGANISMS\*\*** | As for ***patients without features of systemic***  ***Compromise :***  piperacillin-tazobactam 4.5 g IV 6 hourly will provide adequate anaerobic cover, if required, other than for suspected or proven *Clostridiodes difficile*-associated diarrhoea or colitis – ADD oral metronidazole for suspected mild to moderate *C. difficle*  If receiving cefepime or ciprofloxacin first-line, add metronidazole 500 mg IV 12 hourly  *Be mindful of the risk of Clostridium difficile when prescribing cephalosporins or ciprofloxacin* |

*\*Ensure a gentamicin therapeutic drug concentration is taken 6-10 hours after administration of dose in case ongoing therapy is required*

*\*\*If multiresistant organisms are noted call Antimicrobial Stewardship (during business hours) or Infecitous Diseases (after hours) for advice*

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| **Note**: **‘systemic compromise’** is defined as one or more of the following:   1. Systolic blood pressure ≤90 mmHg, or ≥30 mmHg below patient’s usual blood pressure unresponsive to fluids, or 2. Requirement for vasopressor support 3. Room air arterial pO₂ of ≤60 mmHg\*, or saturation ≤92%\*, or requirement for mechanical ventilation 4. Confusion or altered mental state\* 5. Disseminated intravascular coagulation\* or abnormal Prothrombin Time (PT)/ Activated Partial Thromboplastic Time (APTT) 6. Cardiac failure or arrthymia\*, renal failure\*, liver failure\*, or any major organ dysfunction\* 7. **Lactate >2**   Organ failure only if new or significantly worsening. Disregard stable congestive heart failure or chronic arrhythmias (such as atrial fibrillation). |

**IB. Additional antimicrobial cover for special circumstances**

##### Previously Isolated Pathogens:

If an organism has been previously isolated from the patient, the antibiotic regimen should be chosen to ensure coverage of this isolate. This should be achieved whilst maintaining at least the above specified cover due to the risk of polymicrobial sepsis. Consultation with the on call Infectious Diseases physician is advised.

##### Evidence or Suspicion of Herpes Simplex Infection:

**aciclovir** 10 mg/kg IV 8 hourly should be added to the regimen

OR

**famciclovir** 500 mg orally twice daily

OR

**valaciclovir** 1 g orally twice daily

##### Evidence of suspicion of Viral Respiratory Pathogen

Flocked swab

Empiric **oseltamivir** 75 mg orally twice daily for 5 days or until excluded by respiratory polymerase chain reaction results

##### Suspected or confirmed Clostridium difficile infection

While awaiting stool cultures, initiate:

vancomycin 125 mg orally 6 hourly

If oral administration not suitable:

metronidazole 500 mg IV 8 hourly

AND

vancomycin 125 mg via enteral tube 6 hourly

Review therapy once stool cultures available, consult Infectious Diseases or Microbiology for interpretation if required. Infectious Diseases involvement recommended if *Clostridium difficile* infection is confirmed.

**IC. Assessment of Progress and Changes in Therapy:**

1. Daily review and modification of therapy with positive cultures:

* The isolation of any organism may be significant. The antibiotic regimen should be chosen to ensure targeted coverage of the isolate while maintaining broad-spectrum coverage - Gram-negative bacilli, in particular *Pseudomonas aeruginosa* should be covered. For example, aminoglycoside may need to be added to the first line broad spectrum antibiotics but first discuss with Infectious Diseases team.
* Confirmed *Staphylococcus aureus* bacteraemia is an indication for a minimum of 2 weeks of intravenous antibiotic treatment with an effective antibiotic (followed by oral antibiotics if indicated) due to high rate of infective endocarditis and osteomyelitis with inadequate duration of treatment. Echocardiography to exclude vegetations should be considered.

1. Review of treatment at day 3 if cultures are negative:

* Patients who are afebrile within 3 days of starting IV antibiotics may be switched to oral antibiotics (as for low risk patients) if there is no discernible focus of infection and there has been clinical improvement.
* If fevers persist or recur after 72 hours from commencement of empirical antibiotics and no obvious localised cause is present, a reassessment for causes of fever (such as antibiotic resistant bacteria, fungi, viruses, or non-infective causes of fever) or non-response (such as infected intravascular device or undrained collection) to antibiotics should be performed.
  + Repeat chest X-ray (and other imaging such as CT scan of chest, abdomen and sinuses if indicated)
  + Echocardiogram either transthoracic or transoesophageal, to exclude vegetation
  + Repeat blood cultures and other relevant cultures
  + Review all previous results.
* Vancomycin, if commenced empirically, should be ceased, regardless of ongoing fever, if patient is not systemically compromised
* Due to lack of evidence of benefit from controlled trials, broadening Gram-positive cover by the addition of vancomycin to patients with ongoing fever at Day 3 is NOT recommended, unless the patient has developed systemic compromise
* Gentamicin, if commenced empirically, should be ceased.
* Consider empirical antifungal therapy if there is evidence of a focal lung lesion or previous episodes of documented suspected/fungal infection. This is instituted in consultation with the Infectious Diseases Team.

1. Review of treatment at day 5-7 if cultures are negative:

* Patients who are afebrile within 5 days of starting IV antibiotics may be switched to oral antibiotics (as for low risk patients) if there is no discernible focus of infection and there has been clinical improvement.
* Persistence of fevers after 5-7 days with adequate broad-spectrum antibiotic cover in the absence of any obvious cause is an indication to consider empirical antifungal therapy with an appropriate agent. This is instituted in consultation with the Infectious Diseases Team. (Above procedures under section 2. Need to be repeated)

#### ID. Guidelines for the cessation of antibiotic treatment

*Criteria for cessation of Empirical Antibiotics:*

Criteria that must be met before empirical antibiotics can be ceased include all of the following:

* Resolution of neutropenia:
  + The neutrophil count should be >0.5 x 109/L and showing a continuing trend towards recovery over the previous 2 days before cessation of antibiotics.
* No current evidence of infection:
  + The patient should be afebrile for a **minimum of 48 hrs** and all foci of infection should be healing. No new infective lesions should have appeared.
* The total minimum duration of treatment is 7 days.

*Cessation of Antibiotic therapy prior to recovery from Neutropenia:*

In some patients, neutrophil recovery may be delayed, or may never recover to normal levels (e.g. myelodysplastic syndromes, resistant AML). Under these circumstances, cessation of antibiotics before recovery of adequate neutrophil counts is recommended only if the following additional criteria are met:

* The daily peak temperature has been <380C for the last 5 days and the patient is otherwise clinically well
* The total minimum duration of treatment is 7 days
* Clinicians may consider discontinuing treatment before the neutrophil count has recovered to > 0.5 x 109 cells/L if the patient can be carefully observed, the mucous membranes and integument are intact, and there is no impending invasive procedure or ablative chemotherapy planned.

**II. Ancillary Treatment**

**II.A Correct Dehydration and Electrolyte Imbalance**

Febrile neutropenic patients tend to have intravascular fluid depletion and renal impairment.

* Dehydration should be corrected with IV fluids
* Dehydration secondary to vomiting or diarrhoea is accompanied by sodium and potassium loss. Therefore consider appropriate electrolyte replacement

Caution is required when prescribing IV fluids. Replace fluids according to results of recent blood tests. Avoid excessively rapid IV fluid replacement as it leads to pulmonary and peripheral oedema. In accordance with current sepsis management guidelines it is recommended an initial rapid fluid bolus of 20-30mL/kg as a STAT. This should be done concurrently with IV antibiotics on arrival

* Vigilant recording of Fluid Balance input and output is required.

**II.B Mucositis**

*Refer to procedure Chemotherapy Care of the Adult Patient (eviQ) located on the CHS Policy Register*

**II.C Nausea and Vomiting**

*Refer to protocols for Post Chemotherapy Monitoring and Support Procedure*

**II.D Diarrhoea**

Patients with suspected or confirmed infectious diarrhoea require contact precautions

* Gloves and gown should be worn while in contact with patient and their belongings or environment
* Hands should be cleaned with an anti-microbial soap and water.

Stool samples should be sent for culture and *Clostridium difficile (C Diff)* toxin testing.

Symptomatic management of non-infectious diarrhoea (after negative result for C Diff has been obtained) can include loperamide 4mg stat following each loose motion (up to a maximum of 16mg per 24 hours).

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| Section 4 – Low Risk Febrile Neutropenia Patient Management |

Timely assessment and treatment are imperative and the follow up guidelines outlined need to be adhered to so as to ensure best patient care. Appropriate assessment of patients as LOW RISK for complications of febrile neutropenia is essential and is conducted by the MASCC criteria (see Section 7).

*Inclusion criteria*

Adult haematology/oncology patients with features suggestive of febrile neutropenia who are currently or have recently received chemotherapy.

*Exclusion criteria*

Systemic compromise either clinically or from formal measurement of vital signs, indicating that the patient has HIGH RISK febrile neutropenia which will require inpatient management.

**Assessment**

All patients presenting with features suggestive of febrile neutropenia require:

1. Assessment of airway, breathing and circulation.
2. Vital signs to exclude haemodynamic compromise, **exclude from out-patient management if:**

* Heart rate < 40 or > 140 beats/minute
* systolic blood pressure < 90 or > 200 mmHg
* Oxygen saturation < 92% in room air
* Modified early warning score (MEWS) > 4
* Altered level of consciousness

1. FBC with WBC differentials, EUC, LFT, blood cultures with 1 set peripherally and 1 set from each lumen of central venous access device if present (or 2 sets peripherally if patients have no central venous access device)
2. Mid-stream urine for Micro culture and Sensitivity (MC&S)
3. Chest X-ray (CXR) **If any respiratory symptoms**
4. Stool MC&S and *C.difficile* toxin if presenting with diarrhoea
5. Further targeted investigations depending on the presentation may include swabs from wound sites or sputum for MC&S.

Out-patient management should be considered for patients with a MASCC score of 21 or greater not withstanding any advice from the consultant involved.

If considered appropriate, patients must:

1. Live within 1 hour or 48km from the clinic/hospital
2. Treating haematologist, oncologist willing to go ahead with out-patient management
3. Be able to comply with regular review
4. Have a support person with them at home ***at all times***
5. Have phone and transport facilities available to them
6. Have no previous history of noncompliance with medications
7. Patient and carer comfortable with plans for out-patient management.

*Approach to the patient*

Once assessed as appropriate for outpatient care, therapy must be commenced within 1 hour of review and documented febrile neutropenia.

Treatment should commence with:

* ciprofloxacin 750 mg orally twice daily

PLUS

* amoxicillin/clavulanate 875 mg/125 mg orally twice daily

In patients hypersensitive to penicillin:

* ciprofloxacin 750 mg orally twice daily

PLUS

* clindamycin 450 mg orally three times daily

Ciprofloxacin should not be used if the patient has been receiving fluoroquinolone prophylaxis during their chemotherapy or if there is a high rate of fluoroquinolone resistance in the population. **\*Be mindful of the risk of *C.difficile* when prescribing cephalosporins or ciprofloxacin.**

If there is a risk/symptom concerning *C.difficile* infection consider treatment with metronidazole 400 mg orally three times daily for 10 days should be considered.

*Ongoing follow up and review of patients receiving outpatient management*

All patients need to be monitored for **1 hour post first dose of antibiotics to ensure no acute reactions or worsening in overall condition.**

**All patients must be reviewed in the clinic the following day to ensure response/no deterioration.**

Daily/frequent phone contact is required to ensure resolution of fever by home thermometer.

Monitor Full blood count (FBC) including white cell count(WCC) differentials to ensure myeloid reconstitution.

Consider in-patient management and changing to intravenous antibiotics if:

1. Persistent neutropenic fever i.e. on-going fevers despite 2-3 days of empiric therapy
2. Fever recurrence.
3. New signs or symptoms.
4. Inability to tolerate oral medications.
5. Need to change or add antibiotics.
6. Microbiology indicates resistance.
7. Documented bacteraemia.

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| Section 5 – Patient Care |

**Patients:**

Neutropenic patients must not share a room with patients treated for or suffering from infectious disease or communicable diseases, a single room is preferred. Patients should be cared for as follows:

1. Continue to monitor vital signs 4-hourly or more frequently in line with MEWS score
2. Do not administer intramuscular (IM) injections or per-rectal (PR) medications
3. Administer antipyretics as ordered by medical officer. But make sure possible masking effect of antipyretics is considered during assessment.
4. Perform a meticulous daily examination to identify any new foci of infection or evidence of progression of previous infective foci
5. Change all IV giving sets every 24 hours. Label and Date the giving sets with the stickers provided
6. Appropriate fluid balance monitoring
7. Check Electrolytes, Urea, Creatinine full blood counts (with white cell differential) and CRP daily. Check Liver Function Tests (LFTs) at least twice weekly
8. Perform CXR weekly or as appropriate to detect any infiltrates, which may not be clinically evident.
9. Order medical imaging such as CT scans as necessary (e.g. evidence of new collections) as dictated by clinical signs and symptoms
10. Echocardiogram if needed
11. For patients prescribed gentamicin, check serum levels of gentamicin according to gentamicin Clinical Procedure. Check trough levels of vancomycin every 48 hours following commencement of therapy and twice weekly thereafter with adjustment of dose levels according to results
12. Check other drug levels such as vancomycin, Posaconazole as appropriate
13. During recovery from neutropenia previous infected sites may begin to suppurate with the return of neutrophils and need to be managed accordingly.

*Personal Hygiene:*

* Encourage personal hygiene by using a mild soap/wash and daily shower
* Discard toothbrush regularly (i.e. at least every three months, or earlier if the toothbrush becomes ‘shaggy’)
* Use electric shaver
* Tampons to be avoided
* Reminder: Females should wipe perineum front to back to prevent urinary infection
* Patients suffering from incontinence should have their skin protected from their excreta by cleaning with soap and water and applying a barrier cream.

**Staff**

* All cytotoxic drugs require a 7 day excretion period
* It is necessary to use appropriate Personal Protective Equipment (PPE) when managing these patients
* Refer to Section 5 Infection, Prevention and Control Strategies of the *Infection Prevention and Control – Healthcare Associated Infections procedure*
* Patients with suspected or confirmed infectious diarrhoea require contact precautions
  + Gloves and gown should be worn while in contact with patient and their belongings or environment.
  + Hands should be washed with an anti-microbial soap and water.
* Staff affected by certain infectious diseases should be absent from work (refer to Section 5.8 Exclusion periods for healthcare workers exposed to or with an infectious condition of the *Infection Prevention and Control – Healthcare Associated Infections procedure*).

**Environment**

* All persons - staff and visitors - must perform hand hygiene (either by using alcohol hand-rub or using soap and water) prior to entering and after leaving the patient’s room, as well as after touching the patient’s equipment. Complete the 5 minute hand hygiene course particularly the staff joining the Haematology Oncology team both short and long term. Logon to the Hand Hygiene Australia Learning Management System under Online Learning Login (Mandatory training for all staff)
* Jewellery and artificial nails should not be worn by healthcare workers (see Infection Prevention and Control Manual).
* Change bed linen every day (clean sheets and pillowcases every day may reduce the risk of acquiring an opportunistic infection)
* Flowers and pot plants are not allowed in the Haematology ward (potential source of bacteria and fungus, signs to remind staff and visitors)
* Wear gloves when handling potentially infectious biologic material. Change gloves between patients or prior to touching a clean surface when soiled
* Daily change of nebulisers and oxygen masks
* Avoid exposure to all sources of stagnant water (mouth care equipment).

**Cleaning**

* Clean room daily, ensuring that surfaces are visibly clean
* Clean high touch areas (e.g. doorknobs, toilet) daily
* Clean walls, blinds, and window curtains of dust on discharge or if patient is in the room greater than 7 days
* Patient fridge should be cleaned weekly and food that is stored in fridge should be dated and removed after 24 hours.

**Visitors**

* Visits by children should be restricted with exception of immediate family
* Visitors who are unwell should not visit.

**Diet:** For specific dietary requirement for patients who are neutropenic please contact the Nutrition Department on ext 42567. Patient information handout for neutropenic dietary advice is available on the CHS Policy Register and named What should I eat while I am neutropenic or my immune system is weakened.

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| Section 6 – Febrile Neutropenia Triage Letter |

Each patient who has received anti-neoplastic agents (chemotherapy) and is likely to be profoundly neutropenic will be given a letter (see Attachment 2). This letter is to be provided to ED upon arrival to ensure neutropenic patients are triaged according to the CHS Emergency Network procedures, and treatment is provided within the timeframes as set out in this procedure.

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| Section 7 – Multinational Association for Supportive Care in Cancer (MASCC) Risk Index |

The Multinational Association for Supportive Care in Cancer (MASCC) risk index is the recommended assessment tool for determining patient risk.

**MASCC index score for identifying low-risk patients with neutropenic fever**

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| **Characteristic** | **Point score** |
| Burden of illness \*   * no or mild symptoms * – moderate symptoms | 5  3 |
| No hypotension  [i.e. SBP > 90mmHg] | 5 |
| No chronic obstructive pulmonary disease  [i.e. No active chronic bronchitis, emphysema, decrease in forced expiratory volumes, and need for oxygen therapy, corticosteroids, and/or bronchodilators.] | 4 |
| Solid tumour  OR  no previous fungal infection [i.e. No demonstrated fungal infection or empirically treated suspected fungal infection] | 4 |
| Outpatient status at fever onset | 3 |
| No dehydration | 3 |
| Aged < 60 years | 2 |

\*Burden of illness: Means overall clinical state as assessed by clinician at time of presentation – categorised qualitatively as “No or mild symptoms”, “moderate symptoms”, “severe symptoms” or “moribund”

The maximum value in this system is 26.

SCORE ≥21 : LOW RISK

SCORE <21 : HIGH RISK

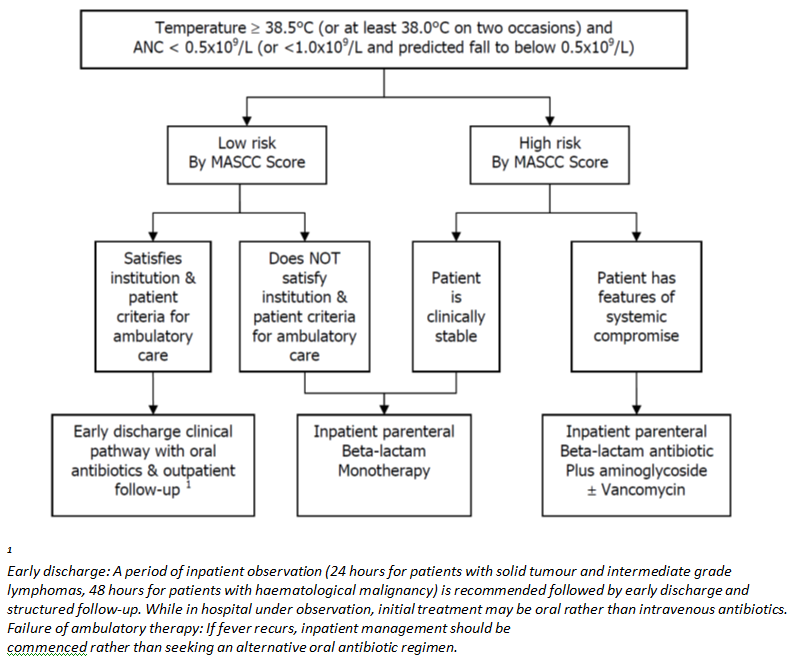
A score of ≥21 predicts a low (≤ 6%) risk for severe complications and a very low mortality (<1%) in neutropenic febrile patients.

In addition to the score, a patient must fulfil ALL of the following to be considered as “low-risk”:

* Appears well
* Normal blood pressure
* No dyspnoea/hypoxia
* Eating and drinking well
* No signs of focal infection.

When a patient has been identified as “low-risk”, then an assessment for eligibility for ambulatory care should also be performed.

**Overview of management as determined by risk stratification (Chart 2)**

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| Section 8 – Management of suspected fungal infection in high risk patients |

This section outlines the approach to patient identification, investigation and management of neutropenic high risks Haematology or Oncology patients who may be at a risk of invasive fungal infection (e.g. *Aspergillus spp*). All patients undergoing investigation for possible invasive fungal infection should trigger an infectious diseases consultation at time of suspicion.

The following patients are considered at-risk for invasive fungal infection:

|  |  |
| --- | --- |
| **Risk Category** | **Risk Factors** |
| **High risk: > 10% incidence of invasive fungal disease** | Neutrophils <0.1 x 109/L for >3 weeks or <0.5 x 109/L for >5 weeks  Unrelated, mismatched or cord blood donor heamatopoietic stem cell transplant (HSCT) Graft Versus Host Disease (GVHD)  Corticosteroid >1mg/kg prednisolone equivalent and neutrophils <1 x 109/L for >1 week  Corticosteroid >2mg/kg prednisolone equivalent for > 2 weeks  High-dose cytarabine +/- fludarabine  Fludarabine use in highly treatment-refractory patients with chronic lymphatic leukaemia (CLL) or low grade lymphomas  Alemtuzumab (particularly in CLL or lymphoma)  Acute lymphoblastic leukaemia (ALL)  Acute Myeloid Leukaemia (AML) |
| **Intermediate risk: 2-10% incidence of invasive fungal disease** | Neutropenia 0.1-0.5 - x 109/L for 3-5 weeks  Neutropenia 0.1-0.5 - x 109/L for <3 weeks with lymphopenia |
| **Low risk: <2% incidence of invasive fungal disease** | Peripheral blood stem cell (PBSC) autologous HSCT  Lymphoma |

Enact the following protocol for **low at-risk** patients if the following are present:

1. Refractory fevers (>5 days despite broad spectrum antibiotics)
2. Focal respiratory or rhino-cerebral symptoms or necrosis on palate (particularly if uncontrolled diabetes)
3. Undifferentiated/unexpected central nervous system symptoms, signs, or imaging

\*Please note undifferentiated skin lesions may also represent disseminated fungal infections\*

**Flow chart-Management of suspected fungal infection in high risk patients**

**Perform all imaging and baseline investigations ideally prior to ID consult unless patient is clinically unwell or there is significant diagnostic uncertainty to warrant earlier review.**

Clinically well/stable (assumed on no/fluconazole/itraconazole prophylaxis as low-risk)

Clinically unwell/unstable regardless of type of prophylaxis

**COMMENCE Empiric Therapy:**

Commence empiric therapy (see Table 2)

**PERFORM Baseline investigations:**

Blood urine, sputum, faeces culture and other sites as necessary (as clinically indicated)

HRCT scan: Chest, sinuses (in all patients). Abdomen or other sites as clinically indicated

GM-ELISA (Serum) and *Aspergillus* PCR (blood EDTA)

**Clinical Suspicion of Invsive Fungal Disease after clinical review and investigation**

**No Clinical Suspicion of Invsive Fungal Disease after clinical review and investigation**

**COMMENCE Treatment:**

Commence empiric therapy if not already commenced (see Table 2)

Consider alternative diagnoses

If empiric therapy commenced: consider ceasing in consultation with Infectious Diseases

**Further investigations management as required:**

Radiological abnormality detected in lung HRCT: lung biopsy or bronchoscopy ideally within 24 hours of CT result

Features of fungal sinus infection on sinus CT: Same day ENT review of images if any Biopsy of other sites as clinically indicated. **RESPIRATORY CONSULT WILL BE REQUIRED IF LUNG ABNORMALITY**

If skin abnormality of concern then skin biopsy

***All samples to be sent for histology, MC&S + fungal culture, Aspergillus +/- panfungal PCR (in consultation with microbiology registrar) fresh, not crushed where possible***

Check for results daily

Adjust empirical therapy according to results in consultation with Infectious Diseases and ward pharmacist

Enact the following protocol for **medium to high at-risk** patients if the following are present:

1. Refractory fevers (>5 days despite broad spectrum antibiotics)
2. Focal respiratory or rhino-cerebral symptoms (particularly if uncontrolled diabetes).
3. Undifferentiated skin lesions thought to be possibly due to disseminated fungal Infection
4. Undifferentiated/unexpected central nervous system symptoms, signs, or imaging

**Flow Chart- Management of suspected fungal infection in medium to hig risk patient if the above are present**

**Perform all imaging and baseline investigations ideally prior to ID consult unless patient is clinically unwell or there is significant diagnostic uncertainty to warrant earlier review.**

Clinically well/stable

Clinically unwell/unstable regardless of type of prophylaxis

On no/fluconazole/itraconazole prophylaxis

On voriconazole, posaconazole or amphotericin B prophylaxis

**Therapeutic** antifungal drug level result in the last 2 days (see Table 1)

**NO** therapeutic antifungal drug level available in the last 2 days

Stay on antifungal prophylaxis AND

**COMMENCE Empiric Therapy:**

Commence empiric therapy (see Table 2)

**PERFORM Baseline investigations:**

Blood urine, sputum, faeces culture and other sites as necessary (as clinically indicated)

HRCT scan: Chest, sinuses (in all patients). Abdomen or other sites as clinically indicated

GM-ELISA (Serum) and *Aspergillus* PCR (blood EDTA)

**No Clinical Suspicion of IFD after clinical review and investigation**

**Clinical Suspicion of IFD after clinical review and investigation**

Consider alternative diagnoses

If empiric therapy commenced: consider returning to previous antifungal prophylaxis in consultation with Infectious Diseases if no further investigation or management for IFD is required

**COMMENCE Treatment:**

Commence empiric therapy if not already commenced (see Table 2)

**Further investigations management as required:**

Radiological abnormality detected in lung HRCT: lung biopsy or bronchoscopy ideally within 24 hours of CT result

Features of fungal sinus infection on sinus CT: Same day ENT review of images if any Biopsy of other sites as clinically indicated.

**RESPIRATORY CONSULT WILL BE REQUIRED IF LUNG ABNORMALITY**

***All samples to be sent for histology, MC&S, Aspergillus +/- panfungal PCR (in consultation with microbiology registrar) fresh, not crushed where possible***

Check for results daily

Adjust antifungal management according to results in consultation with Infectious Diseases and ward pharmacist

**Table 1: Antifungal Drug Levels**

|  |  |
| --- | --- |
| **Prophylactic Therapy** | **Therapeutic Level** |
| **Fluconazole** | Therapeutic drug levels do not apply to the management of presumed mould infection |
| **Intraconazole** | NA – we do not use |
| **Voriconazole** | >1 - < 5.5 mg/L |
| **Posaconazole** | > 0.7 mg/dL (prophylaxis) and >1.2 mg/dL (therapy) |

**Table 2: Empiric Therapy Agents**

|  |  |  |
| --- | --- | --- |
| **Clinical Assessment** | **Therapy** | **Agent to choose for empiric therapy** |
| **Stable** | **No/fluconazole/itraconazole** | Liposomal amphotericin B at 5mg/kg TBW  Anidulafungin or voriconazole could be considered but please discuss with Infectious Diseases if this approach is taken. |
| **Voriconazole** | Liposomal amphotericin B at 5mg/kg TBW |
| **Posaconazole** | Liposomal amphotericin B at 5mg/kg TBW |
| **Prophylactic liposomal Amphotericin B** | Liposomal amphotericin B +/- other agents.  Discuss case with Infectious Diseases in addition to prescribing amphotericin. |
| **Unstable or presumed central nervous system involvement** | **Any with clinically unstable disease** | Liposomal amphotericin B minimum5mg/kg – if going to ICU or CNS disease consider whether higher dosing (10mg/kg) may be required in conjunction with Infectious Diseases. |
| **Any with suspicion of *Lomentospora sp. (usually determined by Infectious Diseases)*** | | Voriconazole as per recommended dose + terbinafine oral 250mg + discuss with Infectious Diseases whether any other agents are required |

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| Evaluation |

**Outcome**

Patient’s who are suspected of having febrile neutropenia are managed as per this procedure

**Measures**

* Review of clinical Incident report data will be reported to and reviewed regularly by the Lead Clinician and divisional Executive Director
* Ongoing surveillance and data capture by auditing of clinical files against the guideline to check compliance. This data captured via the Cancer and Ambulatory Services (CAS) Patient Quality Safety Report and Mortality and Morbidity Reports, is presented on a monthly basis at the CAS Clinical Governance Committee

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| Related Policies, Procedures, Guidelines and Legislation |

**Policies:**

* Patient Identification - Pathology Specimen Labelling Policy
* Nursing and Midwifery Board of Australia (NMBA) Requirements for Practice
* Informed Consent – Clinical Policy

**Procedures**

* Blood Culture Collection procedure excluding neonates
* Central Venous Access Device (CVAD) Management – Children, Adolescents and Adults (NOT Neonates) Procedure
* Patient Identification and Procedure Matching Procedure
* Vital Signs and Early Warning Scores Procedure
* Infection Prevention and Control- Healthcare Associated Infections
* Chemotherapy Care of the Adult Patient
* Protocols for Post Chemotherapy Monitoring and Support Procedure

**Legislation:**

* *Health Records (Privacy and Access) Act 1997 (ACT)*
* *Medicines, Poisons and Therapeutic Goods Act* 2008 (ACT)
* *Human Rights Act 2004*

**Other**

* Australian Charter of Health Care Rights

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* Oncology item- Treatment Protocol (02-1043.1)
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11. Therapeutic Guidelines, 2021 https://www.tg.org.au/

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| Definition of Terms |

**Febrile Neutropenia:**

Temperature greater than or equal to 380C

Absolute Neutrophil Count (ANC) < 1x109/L (or assumed until proven otherwise with a previous history of chemotherapy)

**ABCD –** Airway, Breathing Circulation and Defibrillation

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| Search Terms |

Neutropenia, Febrile neutropenia, FN call, Emergency Department Febrile Neutropenia, Patient Management, High risk Febrile Neutropenia Patient Management, Low risk Febrile Neutropenia Patient Management, Febrile Neutropenia Triage Letter, Neutropenic Diet, MASCC risk index

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| Attachments |

Attachment 1: Triages and antibiotic administration guide

Attachment 2: Febrile Neutropenia Triage Letter

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**Disclaimer**: *This document has been developed by Canberra Health Services specifically for its own use. Use of this document and any reliance on the information contained therein by any third party is at his or her own risk and Canberra Health Services assumes no responsibility whatsoever.*

*Policy Team ONLY to complete the following:*

|  |  |  |  |
| --- | --- | --- | --- |
| *Date Amended* | *Section Amended* | *Divisional Approval* | *Final Approval* |
| *18 January 2022* | *Complete Review* | *Kath Wakefield, ED-CAS* | *CHS Policy Committee* |
|  |  |  |  |

*This document supersedes the following:*

|  |  |
| --- | --- |
| *Document Number* | *Document Name* |
| *CHHS18/051* | *Febrile Neutropenia Management* |
|  |  |

## Attachment 1: Triage scale and antibiotic administration guide

|  |  |  |
| --- | --- | --- |
| **TRIAGE CATEGORY 2**  is to be allocated to all patients presenting with symptoms of suspected febrile neutropenia (recent chemotherapy and T>380C) given risk of septic shock and mortality rate of 2.2% | | |
| **Inclusion Criteria** | | **Exclusion Criteria** |
| Adult patient with:   * Haematology / oncology patient **and** * Chemotherapy in last 21 days (or bone marrow transplant past 3mths) **and** * Temperature >380C | | **Cease Procedure** and **notify senior medical officer immediately** if:   * ABCD compromise * patients with known normal WCC within previous 24hrs – follow this SOP if neutropenic in ED |
| **Assessment** | **Intervention** | |
| **WH&S** | Reverse barrier nurse in isolation room (if available – do not delay treatment if unavailable), avoid staff /visitors with infection | |
| **Airway:** Assess patency | Monitor and maintain airway patency | |
| **Breathing:** RR / SaO2 | Administer O2 – maintain SaO2 >94% | |
| **Circulation:** HR / BP | Record vital signs – calculate MEWS | |
| **Investigations:**  Pathology  pathology requests are at Medical Officer’s discretion  Radiology | *FBC, UEC, Coags (FCP), LFTs, CRP*  *Blood Cultures (BC) x 2 different venepuncture sites (prior to commencement of antibiotics if possible)*   * if CVC insitu collect extra BC from each lumen of CVC * *follow procedure for accessing CVC* * *do not flush lumens prior to withdrawal of blood* * *use initial draw / sample of blood for BC*   *Septic screen*   * Mid-stream urine – all patients * Stool Culture including C. difficile – if diarrhoea * Sputum Culture – if productive cough * Respiratory Virus screen – if respiratory signs and symptoms * Swab intravenous access sites, wounds, suspicious lesions – if redness, pain, or discharge * CXR – all patients (Medical Officer) | |
| **Treatment:**  **URGENT** antibiotic therapy regime – within **30mins** of presentation | **Time critical antibiotic administration required** within **30mins** of presentation (Medical Officer - see guide below)  **Do not delay administration of antibiotics while waiting for results of pathology investigations** | |
| **Monitor:** Vital signs | Monitor vital signs / calculate MEWS frequently / record fluid balance chart | |
| **Comfort:** Record pain  0 = pain free, 10 = excruciating  Nausea / vomiting | *Offer analgesia as per Medication Standing Orders*  *Offer analgesia as per Medication Standing Orders* | |
| **Document:** | Document in medical record / enter ‘Time Seen’ in EDIS | |

**Note*:*** *Highlighted* clinical treatment or procedures above extend standard scope of practice for nursing staff and therefore require relevant competency accreditation in the Emergency Department

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| --- | --- |
| **Patient group** | **Recommended Antibiotic Therapy (doses for normal renal function)** |
| **Patients without features of systemic**  **Compromise AND NO KNOWN PAST HISTORY OF ANTIMICROBIAL RESISTANT ORGANISMS\*\***  (Beta-lactam monotherapy is recommended  Unless patient hypersensitive to the recommended medicine) | **No penicillin allergy:**  gentamicin IV once daily stat according to CHS protocol\*  PLUS  piperacillin-tazobactam 4.5 g IV 6 hourly |
| **Non-life threatening penicillin allergy (rash):**  gentamicin IV once daily stat according to CHS protocol\*  PLUS  cefepime 2 g IV 8 hourly |
| **Life-threatening (immediate) penicillin allergy or**  **beta-lactam allergy:**  gentamicin IV once daily stat according to CHS protocol\*PLUS  vancomycin IV according to the Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines follow links to the antibiotic, febrile neutropenia section |
| **Patients with systemic compromise** | meropenem 1 g IV eight hourly  PLUS  vancomycin IV according to Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines site follow links to the antibiotic, febrile neutropenia section |
| **Patients with obviously**  **infected vascular devices, or MRSA carriers with extensive skin breaks / desquamation** | As for ***patients without features of systemic compromise***  PLUS  vancomycin IV according to Therapeutic Guidelines Managing Patients with Febrile Neutropenia on the Therapeutic Guidelines site follow links to the antibiotic, febrile neutropenia section. |
| **Patients with features of abdominal or**  **perineal infection AND NO KNOWN PAST HISTORY OF ANTIMICROBIAL RESISTANT ORGANISMS\*\*** | As for ***patients without features of systemic***  ***Compromise :***  piperacillin-tazobactam 4.5 g IV 6 hourly will provide adequate anaerobic cover, if required, other than for suspected or proven *Clostridiodes difficile*-associated diarrhoea or colitis – ADD oral metronidazole for suspected mild to moderate *C. difficle*  If receiving cefepime or ciprofloxacin first-line, add metronidazole 500 mg IV 12 hourly  *Be mindful of the risk of Clostridium difficile when prescribing cephalosporins or ciprofloxacin* |

**\***Note: **‘systemic compromise’** is defined as one or more of the following:

1. Systolic BP ≤90 mmHg or ≥30 mmHg below patient’s usual BP, or reqt for vasopressor support

2. Room air arterial pO2 of ≤60 mmHg, or SaO2 ≤90%, or requirement for mechanical ventilation

3. Confusion or altered mental state 4. Disseminated intravascular coagulation or abnormal PT/APTT

5. Cardiac failure or arrythmia, renal failure, liver failure, or any major organ dysfunction [Organ failure only if new or significantly worsening. Disregard stable congestive heart failure or chronic arrhythmias (such as AF)]

## Attachment 2: Febrile Neutropenia Triage Letter

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| **Febrile Neutropenia**  **Triage Letter** |

**Attention Triage Nurse / ED doctor:**

Dear Nurse / Doctor,

Type of Chemotherapy given:

This patient has recently received anti-neoplastic agents (chemotherapy) and is likely to be profoundly neutropenic.

Infection is the most common complication associated with febrile neutropenia and accounts for substantial morbidity. It can be fatal within a short period of time if not treated immediately.

The Canberra Hospital Policy defines neutropenia as an Absolute Neutrophil Count of <1 X 109/L. A neutropenic fever is defined as an oral temperature of greater than or equal to 380C.

A patient who has a fever and a history of receiving anti-neoplastic agents in the last 21 days should be assumed to be neutropenic until proven otherwise.

Neutropenic patients with infection can present afebrile or even hypothermic.

**This patient is to be triaged as Category 2.**

Assessment and treatment with IV antibiotics is to be commenced within 30 minutes.

Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

1. Please refer to the policy, protocol, and procedure for Febrile Neutropenia

Management.

2. Notify Haematology/Oncology Cover Registrar and/or Consultant for possible admission to Haematology/ Oncology Unit

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