CLINICAL POLICY

NEUTROPENIC FEVER AND NEUTROPENIC SEPSIS - PREVENTION AND MANAGEMENT

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1.0 Introduction

Neutropenic sepsis is a potentially life threatening complication of cancer chemotherapy. All patients should be assessed in a unit familiar with its management and, where appropriate, commence broad-spectrum antibiotics as soon as possible. Despite the previous widespread use of intravenous antibiotics there is increasing recognition that subsets of patients with neutropenic fever without physiological signs of sepsis run a relatively benign course and can be treated with less intensive approaches including antibiotic monotherapy, early hospital discharge and oral antibiotics. These 'low risk' cases typically represent half of patients presenting to the Trust after receiving conventional doses of modern chemotherapy.

2.0 Purpose

This policy has been developed to ensure that patients with neutropenic sepsis receive gold standard care at the Trust.

3.0 Scope

This policy covers the treatment of neutropenic fever and neutropenic sepsis within the Trust.

4.0 Responsibilities

Antimicrobial Stewardship Group – Audit policy to ensure that standards are upheld.
Chemotherapy Nurses – Patients should
  • be counselled about the signs and symptoms of neutropenic sepsis
  • receive the appropriate systemic anticancer treatments leaflet
  • be advised when to contact the hot-line service
  • be advised about temperature monitoring

Chemotherapy prescribing doctors or non-medical prescribers – should ensure all patients are counselled on the importance of taking their temperature etc.

Consultants – To provide support and mentorship to junior staff, follow guidance within policy, embrace prudent antimicrobial prescribing and to lead practice.
Junior medical staff – To ensure that patients are seen and, if appropriate, started on antibiotics within 1 hour, ensure that patients with solid organ tumours with neutropenic fever without sepsis are appropriately MASCC scored (Appendix A), using the “Adult Sepsis and Neutropenic Fever Admission Pathway” proforma (Appendix B), guide taking of appropriate samples for culture and undertake prudent prescribing of antimicrobials. Patients with sepsis should receive antibiotics and intravenous fluid as a bolus for resuscitation within 1 hour.

Nurses with PGD training – To assess patients on admission using the neutropenic sepsis admission assessment proforma (Appendix B) and to administer first line antibiotics to patients if appropriate. Nurses must refer to a suitable medic or non-medical prescriber if the patient is excluded for any reason.

Pharmacists – To ensure patients receive comprehensive pharmaceutical care, ensure antimicrobials prescribed are appropriate, ensure that therapeutic drug monitoring is undertaken when necessary, ensure that patients are counselled on the use of antimicrobials and facilitate prudent antimicrobial prescribing.

Hot-line nurses – To use the UKONS assessment tool (see Appendix C) to ensure that patients are appropriately referred to a hospital within the network.

Acute Oncology ANP - To ensure that patients are seen and, if appropriate, started on antibiotics within 1 hour, ensure that patients with neutropenic fever without sepsis are appropriately MASCC scored (Appendix A), take appropriate samples for culture and undertake prudent prescribing of antimicrobials. Patients with sepsis (or serum venous lactate ≥ 2 mmol/L) should receive antibiotics and intravenous fluid as a bolus for resuscitation within 1 hour.

Ward Nurses – To ensure that patients with neutropenic fever and or sepsis receive their antibiotics within 1 hour, ensure that patients have their blood cultures and any other clinical samples taken before antibiotics are given and ensure that observations are carried out as directed. Ensure that patients are given PGD antibiotics if required or accessing junior medical staff if appropriate.
5.0 Laws & Regulations

The Health and Social Care Act 2008 and associated code of practice requires that organisations have and adhere to policies that will help to prevent and control infections including: antimicrobial prescribing, local formulary and procedures in place to ensure prudent prescribing and antimicrobial stewardship.

NICE guidance CG 151 was published in September 2012, Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients. This guidance was reviewed by the Acute Oncology specific group and the Antimicrobial Stewardship Group. Some recommendations from this clinical guidance have not been followed after careful consideration by the groups above. Key differences are:

Patients are risk assessed on admission stratifying patients into low and high risk earlier; antibiotics are tailored to the patient earlier

High risk patients are given gentamicin along with piperacillin/tazobactam standard due to current microbe sensitivities in the area

Low risk patients (i.e. patients with low risk neutropenic fever without sepsis) are given oral antibiotic from the beginning of their treatment, reducing their exposure to antimicrobials.

Neutropenia is classified as less than or equal to 1.0 x 10⁹/l

The decision to not follow some specific aspects of the NICE guidance was previously fully risk assessed, and the current authors agree that its findings still apply. This risk assessment can be found in Appendix D.

6.0 Definitions

Antimicrobial stewardship - Antibiotic stewardship is designed to optimise antimicrobial therapy administered to hospitalised patients, to ensure cost-effective therapy and improve patients' outcome while containing bacterial resistance.

Neutropenic fever - Temperature ≥ 37.8°C on at least 1 occasion as measured by the patient at home or CCC staff AND neutrophil count of ≤ 1.0 x 10⁹/l without signs of sepsis.

Neutropenic sepsis - Temperature ≥ 37.8°C on at least 1 occasion as measured by the patient at home or CCC staff AND neutrophil count of ≤ 1.0 x 10⁹/l with signs of sepsis.
MASCC Score - Multinational association for Supportive Care in Cancer Scoring system for the proposed risk index for identifying low-risk febrile neutropenic patients. Please note that this is NOT routinely used for patients with haematological cancers.

Neutropenia - neutrophil count of \( \leq 1 \times 10^9/l \). The Antimicrobial Stewardship Group has adapted the existing definition of neutropenic sepsis. The group was concerned that applying NICE definition (neutrophil count \( 0.5 \times 10^9/l \) or lower and temperature \( >37.9^0C \) might lead to under treatment of a significant proportion of patients with neutropenic sepsis (See Appendix D).

Patient Group Directions – mechanisms for the administration of medicines by a health care professional when a patient fulfils agreed criteria.

Low risk neutropenic fever
Solid organ tumour patients who score >21 on the Multinational association for Supportive Care in Cancer Scoring system (MASCC) are considered to be at low risk of developing sepsis and associated death following treatment of neutropenic fever. A patient who is at a low risk of sepsis can still however develop sepsis and the risk of death is therefore increased if sepsis has developed. All patients with signs of sepsis are therefore managed as being at high risk of death.

7.0 Main Body of Policy
7.1 Background to policy
Evidence that prompt use of broad spectrum antibiotics significantly reduce mortality in patients with neutropenic sepsis, in the review by National Confidential Enquiry into Patient Outcomes and Death, For better, for worse? It highlighted that antibiotics should be given within an hour of presentation.

Two large randomised studies of low risk febrile neutropenia have shown equivalence of inpatient oral antibiotics versus inpatient intravenous antibiotics (Friefield et al, Kern et al). Additional research at CCC, (Innes et al) has shown similar efficacy and safety of oral antibiotics combined with early discharge of patients with solid organ tumours and low risk febrile neutropenia.
The Multinational Association for Supportive Care in Cancer (MASCC) risk index (see Appendix A) accurately identifies patients at low risk for complications of neutropenic sepsis (Klastersky et al).

The National Early Warning Score (NEWS – previously known as MEWS) is a simple aggregate scoring system to cover ALL in-patients. The system should be linked to a response team that is appropriately skilled to access and manage clinical problems. All nursing staff are expected to be competent in the use of NEWS in order to predict patients at risk of clinical deterioration and/or cardio-pulmonary arrest.

The “Adult Sepsis and Neutropenic Fever Admission Pathway” proforma provides guidance for management during the first hour of admission (Appendix B). This proforma should be used by both oncology nurses and prescribers involved in providing care to any patients with suspected neutropenic sepsis.

7.2 Education of Patients Receiving Chemotherapy

All patients will be alerted to the risk of neutropenic sepsis at the initial visit for the first cycle of chemotherapy. Patients will be advised to contact the Hot-line service on developing a fever (greater than 37.5°C) during the course of treatment and that it may be necessary to attend hospital for further assessment or admission.

Refer to Chemotherapy telephone Hot-line Policy PCHATTRI and UKONS Triage Assessment Tool (Appendix C).

Patients who attend CCC and satellite clinics for treatment are advised to contact CCC for advice or admission. Patients who attend St Helens (Lilac Centre) are routinely advised to contact the Lilac Centre for advice or admission during working hours. Out of hours, Lilac Centre patients are advised to contact the CCC hot-line service for advice.

7.3 Admission procedure

7.3.1 Diagnosis of neutropenic sepsis

The following patients should be considered at highest risk of neutropenic sepsis:

- Patients with solid organ tumours who have had chemotherapy in the last 6 weeks
- Patients with haematological malignancy who have had chemotherapy within the last 3 months
- Patients who have had an autologous bone marrow transplant within the last 3 months OR an allogeneic bone marrow transplant within the last 12 months (or longer if they remain on immunosuppression) should be managed as neutropenic sepsis even if the neutrophil count is normal.

Patients may not always mount a temperature response due to the severity of their illness. If a patient is unwell on assessment with a history of receiving systemic anticancer therapies, neutropenic sepsis should be suspected. The CCC sepsis screening tool should be completed for all patients who are unwell or present with a NEWS 2 of 5 or more, or with 1 parameter scoring a 3 on NEWS2.

All patients who may have infection and are found to have a serum lactate of 2 mmol/L or more as a result of the sepsis screen should be considered to have sepsis until proven otherwise and receive antibiotics and a fluid bolus within 1 hour.

Not uncommonly, patients present with low grade fever or low WBC that does not fulfil the strict definition of neutropenic sepsis (see section 6.0). Management should be individualised led by a senior clinician (specialist registrar or above) with medical microbiology advice if appropriate.

If patients present with signs and symptoms of sepsis but do not meet the above diagnosis of neutropenic sepsis (i.e. patients with solid organ tumours who received chemotherapy greater than 6 weeks ago), please refer to the trust antibiotic formulary sepsis guidelines: [https://secure.rlbuht.nhs.uk/sites/Antibiotic/SitePages/HomePage.aspx](https://secure.rlbuht.nhs.uk/sites/Antibiotic/SitePages/HomePage.aspx)

7.3.2 Initial assessment and investigations

TREATMENT FOR NEUTROPENIC SEPSIS MUST BE INSTIGATED WITHIN ONE HOUR OF ADMISSION. Antimicrobials are to be given within one hour for all patients. Patients with sepsis must receive all other elements of sepsis six.

Time of arrival is recorded when the patient is admitted onto the ward’s bed list electronically on Meditech and the time is also recorded when the first set of vital signs are taken. All patients with suspected neutropenic fever or sepsis should undergo clinical assessment (“Adult Sepsis and Neutropenic Fever Admission Pathway” proforma – Appendix B), and have the following investigations performed:

- Full blood count and differential;
• Electrolytes, liver function (including albumin), creatinine, random blood glucose, CRP, venous lactate
• A minimum of one set of peripheral venous blood for aerobic and anaerobic cultures, in addition to cultures via a central venous access device if present
• Chest x-ray
• Other Cultures where clinically indicated

7.4 Risk assessment of patients
All patients with suspected neutropenic sepsis should be assessed using the neutropenic sepsis admission assessment proforma on Meditech (Appendix B) and assigned to a risk index. The decision whether to use the high risk management algorithm (Figure 1) should be based on the following:

1. Presence of haematological malignancy
   All patients with haematological malignancy should be managed using the high risk management algorithm (7.5.1.1).

2. Features of sepsis
   The assessment proforma on Meditech can be used to determine whether patients meet physiological criteria for sepsis. Any patients who exhibit at least 2 of the following signs should be managed using the high risk management algorithm (7.5.1.1).
   • Temperature ≥ 37.8
   • Temperature < 36°C
   • Respiration rate > 20 bpm
   • Heart rate > 90 bpm
   • WBC < 4 or > 12 (x10⁹/L)
   • Systolic blood pressure < 100mmHg
   • New altered conscious/confusion level

3. MASCC score
   All patients with a MASCC score (Appendix A) of less than 21 should be managed using the high risk management algorithm (7.5.1.1).

4. Clinician assessment
In patients who do not meet the strict criteria for neutropenic sepsis but look and/or feel unwell, MASCC scoring (Appendix A) may not detect the severity of their illness so if in doubt they should be treated using the high risk management algorithm (7.5.1.1).

7.5 Treatment
Choice of antibiotic is only one part of the management of sepsis. The Surviving Sepsis campaign “Sepsis 6” guidance (see 7.5.1.1) should be followed. Patients should be managed in the step-up beds if indicated following clinical assessment by the Critical Care Nurse Practitioners and/or Registrar. All patients with NEWS2 score of 5 or more should be considered for management in the step up beds. Out of hours this will be the Hospital at night team. All patients with NEWS 2 score of 5 or more, or 3 in 1 parameter, must be reviewed by the SpR on call within 1 hour.

7.5.1 Antibiotic Treatment Protocols
The prescriber should always be aware of potential cautions, contraindications and dose adjustments when prescribing antibiotics. Appendix E contains links to the British National Formulary (BNF) pages for further information.

Nurses who have undergone PGD training and additional training for use of the neutropenic sepsis PGD’s may administer first line low risk or first line high-risk antibiotics. If patients do not meet the criteria for these PGD’s they must be seen by a doctor or a suitable non-medical prescriber as soon as possible. Medical assistance should be always sought if required. After administration of PGD antibiotics patients should also see a doctor as soon as possible.

Choice of antibiotics will be determined by risk score identified by the above assessment, and can be divided into high risk and low risk. Where any doubt exists, it is preferable to manage patients as high risk in the first instance.
7.5.1.1 High risk (including all haem-onc)

**NEUTROPENIC FEVER AND SEPSIS ARE EMERGENCIES**
Management of haem-onc patients & high risk solid organ patients

### Sepsis Six Management Bundle
**MUST** be completed within 1 hour:
1. Administer oxygen to maintain SpO2 at >94%
2. Take blood cultures and consider infective source
3. Administer intravenous antibiotics
4. Consider intravenous fluid resuscitation
5. Measure serial serum lactate
6. Commence hourly urine output measurement

### Baseline Investigations
**SAMPLING & CULTURES MUST NOT DELAY ANTIBIOTIC ADMINISTRATION (60 minutes)**
- Blood / Sputum / Urine for C&S / Peripheral Glucose
- Central Line blood cultures from each lumen
- Respiratory virus PCR swabs.
- Throat swab
- Stool Culture if Diarrhea
- CRP
- Full blood count
- Clotting profile, pro-thrombin time and INR
- Urea and electrolytes
- Liver function tests
- Serum lactate
- Arterial OR Venous blood gas
- Chest X-ray
- **CHECK ALLERGY STATUS**

### First Line antibiotics (no known allergies or other complicating factors)
- IV PIPERACILLIN/TAZOBACTAM 4.5 grams every 6 hours
- AND once daily GENTAMICIN using gentamicin chart (see Appendix F) for NO LONGER than 48 hours then review

### Penicillin allergic patients without a proven history of anaphylaxis
- IV MEROPENEM 1 gram every 8 hours
- AND once daily GENTAMICIN using gentamicin chart (see Appendix F) for NO LONGER than 48 hours then review

### Penicillin allergic patients with a proven history of anaphylaxis
- IV AZTREONAM 2 grams every 8 hours
- AND IV TEICOPLANIN 12mg/kg (rounded up to nearest 200mg) every 12 hours for 4 doses, then adjust dosing (see Appendix G)
- AND once daily GENTAMICIN using gentamicin chart (see Appendix E) for NO LONGER than 48 hours then review

### Are either of the following present?
- Known colonisation with Methicillin-resistant Staphylococcus aureus (MRSA)
- Clinical features of line infection – *any of:* Erythema (redness), induration (firmness or swelling) tenderness or purulent discharge within 2cm of an intravenous catheter (e.g. PICC, Hickman) exit site, overlying Portacath pocket or along tunnel / path of catheterised vein

### If not already prescribed, commence TEICOPLANIN in addition to the above antibiotics
- TEICOPLANIN 12mg/kg (rounded up to nearest 200mg) every 12 hours for 4 doses, then adjust dosing (see Appendix G).

### If after delivering the Sepsis Six, the patient still has any of the following:
- Systolic B.P <90 mmHg
- Reduced level of consciousness despite resuscitation
- Lactate not reducing
- Respiratory rate over 25 breaths per minute

Then call Critical Care Outreach immediately!!

Caution with GENTAMICIN DOISING in patients with known RENAL INSUFFICIENCY. Patients with an eGFR <20ml/min who either have MYELOMA or have been given CISPLATIN should be discussed with on-call haematologist or oncologist respectively before giving GENTAMICIN.

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**Author:** Alex Howard & Lauren Williams  
**Authorised by:** Drug & Therapeutics Committee  
**Copy No:**
Notes

- For patients with a pulmonary source of infection, **add atypical cover with clarithromycin 500mg orally every 12 hours**.
- For patients with a severe penicillin allergy and an intra-abdominal source of infection, **add anaerobic cover with metronidazole 400mg orally every 8 hours** (this does not need to be added if the patient is already on piperacillin/tazobactam or meropenem).

7.5.1.2 Low risk neutropenic fever

Low risk antimicrobials should only be considered for well and stable patients with solid organ tumours who do not meet any of the criteria detailed in the risk assessment in section 7.4 of this document and have no signs of sepsis. Patients who are unable to take oral medication should be managed using the antibiotic choices

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<tr>
<td>Penicillin allergy and no other complicating factors</td>
<td>Oral doxycycline 200mg daily and ciprofloxacin 750mg twice a day for 5 days</td>
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<tr>
<td>Patients unable to take oral medication with no allergies</td>
<td>IV tazocin 4.5 grams four times a day for 5 days</td>
</tr>
<tr>
<td>Patients unable to take oral medication with a penicillin allergy and no other complicating factors</td>
<td>IV aztreonam 2 grams every 8 hours AND IV teicoplanin 12mg/kg (every 12 hours for 4 doses then adjust dosing) (see Appendix E)</td>
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7.5.2 Antibiotic Modification

Patients who remain clinically stable with persisting fever should remain on first line antibiotics for a minimum of 48-72 hours as it is well recognised that fever may take 72 hours or more to resolve despite appropriate antibiotic treatment.

Contact medical microbiology if:

- The patient's clinical condition is deteriorating
- The patient is known to be colonised with resistant gram negative organisms (CPE, ESBL, ciprofloxacin or gentamicin resistance)
• There is a clear clinical focus of infection (e.g. chest, urine, biliary)
• Organisms are grown in clinical specimens (e.g. blood, urine)
• Stable patients continue to have fever despite 72 hours of appropriate antimicrobial therapy (antifungal treatment may be considered).

7.5.4 Prophylactic Antibiotics

7.5.4.1 Patients with haematological malignancy

Please refer to ‘Prophylaxis of infection in neutropenic / immunocompromised Haematological oncology patients’ (SCTCTU-CLIN-08).

7.5.4.2 Patients with solid organ malignancy

The use of prophylactic antibiotics following cytotoxic chemotherapy can result in a small reduction in febrile episodes but at the expense of side effects and potential risk of inducing antibiotic resistance and increasing the risk of clostridium difficile infection. The use of prophylactic antibiotics is therefore not recommended routinely but should be reserved for patients thought to be at particularly high risk of infection. For these high risk patients the following may be used:

• Ciprofloxacin 500mg PO once daily on days 9-20 post chemotherapy dependent on nadir

7.6 Inpatient Monitoring and Escalation

The registered health care professional assigned to the care of ward patients is accountable for the following:

Patients should have full blood count, renal function and electrolytes monitored daily whilst an inpatient.

On admission, baseline vital signs must be recorded on CCC’s NEWS chart and carried forward to each new sheet. A NEWS score must also be documented on Meditech. A NEWS score should be calculated every time vital signs are recorded (refer to Deteriorating patient Escalation Policy PCAPESDET).

Elevated NEWS scores will affect the frequency of observations and the actions to be taken (see Escalation policy for the deteriorating patient PCAPESDET). In patients with
early sepsis (SIRS), observations should be performed every 4 hours as a minimum. Patients with severe sepsis will require hourly observations as a minimum.

7.7 **Discharge**

Patients who have been septic on admission should continue to be managed as high risk once their condition has stabilised.

7.7.1 **Low risk patients**

Patients on oral antibiotics may be considered eligible for discharge if:

- The first dose of antibiotic has been taken and ingestion witnessed by nursing staff.
- Clinically stable and asymptomatic, irrespective of neutrophil count
- Able to comply with the treatment course willing to return to the ward at short notice in the event of antibiotic intolerance or clinical deterioration

Patients without a clear focus of infection will be discharged with sufficient oral antibiotics to complete a 5 day course. For patients with a clear focus of infection, the duration of antibiotics will be determined by the discharging clinician with the advice of the consultant in medical microbiology where appropriate.

7.7.2 **High Risk Patients**

These patients will be assessed daily as above and will be eligible for discharge when clinically improved, afebrile for 24 hours with a rising neutrophil count, irrespective of the absolute value. For patients with a clear focus of infection, the duration of antibiotics will be determined by the discharging clinician with the advice of medical microbiology where appropriate. When the focus of infection has not been elucidated the duration of antibiotics will be determined by the discharging clinician on daily clinical review. Discontinuation of antibiotics before completing a 5 day course may be considered if the patient has a temperature of ≤37.5°C for 24 hours, is well and the neutrophil count is more than 0.5 and rising.

8.0 **Training**

All medical staff are made aware of the neutropenic sepsis policy during induction. Nurses on the wards will be familiarised on induction.

Pharmacists will be made aware of the policy on joining the Trust.
9.0 Audit

9.1 Quality and Risk Standards

a) How the suspected sepsis assessment proforma is completed
   Defined in policy section 7.3 Risk assessment of patients

b) The time from identification of potential in hospital sepsis to administration of antibiotic therapy
   Defined in policy section 7.2 Admission procedure

c) The time of medical assessment / examination documented in medical notes to ensure sepsis bundle compliance
   Defined in policy section 7.3 Risk assessment of patients

d) carrying out the Early Warning Score
   Defined in policy section 7.3 Risk assessment of patients

e) collection of blood culture samples / CXR / appropriate blood samples
   Defined in policy section 7.2 Admission procedure

f) How the compliance with the above will be monitored by the Trust
   An audit will conducted annually to assess performance against the documented process (a - f) detailed above.

Source of Evidence: A case note review of all patients admitted with a diagnosis of Neutropenic sepsis or who develop neutropenic sepsis as an inpatient over a six month period will be conducted to ascertain whether the documented processes A to F have been followed.

Lead: Acute Oncology Chair

Monitoring Committee: Acute Oncology Site Reference Group

Where non-compliance is identified action plans will be developed by the Acute Oncology Chair and progress against the action plan will be presented to the Acute Oncology SRG at each meeting until the issue is resolved.

10.0 References


Friefield et al., A double blind comparison of empirical oral and intravenous antibiotic therapy for low risk febrile neutropenia patients during cancer chemotherapy *NEJM* 1999, 341, 305-11


Kern et al., Oral versus intravenous empirical antibiotic therapy for fever in patients with granulocytopenia who are receiving cancer chemotherapy. *NEJM* 1999, 341, 312-18


11.0 Appendices
Appendix A: MASCC Scoring Index

Multinational association for Supportive Care in Cancer Scoring system for the proposed risk index for identifying low-risk febrile neutropenic patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of illness:</td>
<td></td>
</tr>
<tr>
<td>Either, no or mild symptoms*</td>
<td>5</td>
</tr>
<tr>
<td>Or moderate symptoms*</td>
<td>3</td>
</tr>
<tr>
<td>Severe symptoms</td>
<td>0</td>
</tr>
<tr>
<td>No hypotension (Systolic &gt;90 mmHg)</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumour/lymphoma or no previous fungal infection</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration (IV fluids not required)</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status at onset of fever</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>2</td>
</tr>
</tbody>
</table>

*Points attributable to burden of illness are not cumulative. The maximum theoretical score is therefore 26.

The authors used a threshold of ≥21 points to define “low-risk”.
### Appendix B: Adult Sepsis & Neutropenic Fever Assessment Proforma (Meditech)

#### Adult Sepsis & Neutropenic Fever

<table>
<thead>
<tr>
<th>Sepsis Actions</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Actions required</em></td>
<td>Check Lactate level</td>
<td>IV access</td>
</tr>
<tr>
<td>Lactate level (mmol/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time lactate result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time antibiotics given</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Features of severe sepsis</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lactate&gt;2mmol/l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (SBP) &lt;90mmHg</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Creatinine&gt;177umol/l, or &gt;4umol/l, above baseline</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Hypo Pao2 &lt;80</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><em>About Patient</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Significant IMI</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Antibiotics in last 7 days?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If Yes, please state</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are allergies to antibiotics?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If Yes, please state</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other allergies</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Fibrid Patient</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is the patient involved in any trials?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><em>Fibric Neutropenia</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><em>Does patient have febrile neutropenia?</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Neut &gt; 1x10^9/l AND Temp &gt; 37.5°C on at least 1 occasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Modified MASC assessment</em></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Age of patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Does patient have symptoms related to this?</em></td>
<td>No</td>
<td>Symptoms</td>
</tr>
<tr>
<td>Does patient have symptoms related to this</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does patient have dehydrated patient IV fluids?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Does patient have hypotension?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Systolic BP &lt;90</td>
<td>Systolic BP &gt;90</td>
<td></td>
</tr>
</tbody>
</table>

#### Examination

- **Temperature**:  | Comment: |
- **Blood pressure** 120/80 | Comment: |
- **Respiratory rate**:  | Comment: |
- **O2 saturations (%)**:  | Comment: |
- **NEWS score**:  | Comment: |

- **Are there a clinician’s clinical focus of infection?** | Yes | No |
  - Cellulitis | Abscess | Central line | Pneumonia | Other |
  - Other |

---

**Issue Date:** 11th September 2020  
**Page:** 20 of 29  
**Filename:** PCLANEUTR  
**Issue No:** 11.0  
**Author:** Alex Howard & Lauren Williams  
**Authorised by:** Drug & Therapeutics Committee  
**Copy No:**
### SEPNS pathway

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Oxygen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>IV fluids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Cultures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>IV antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Lactate level and bloods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Urine output</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>NEWS every 30 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Repeat LACTATE 1 Hour after first step up</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Refer to ITU

- Lactate fails to improve or continues to deteriorate
- Hypotension resistant to fluid challenge

<table>
<thead>
<tr>
<th>Decision to transfer patient made</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decision made by Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time decision made</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continue with aggressive fluid resuscitation until transfer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient transferred to</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Decision NOT to transfer patient made
- Decision made by Grade
- Time decision made
- Continue with fluid resuscitation and antibiotics
- Review antibiotics every 48 hours
- Maintain urine output > 0.5ml/kg/hr
## Appendix C – UKONS Triage Assessment Tool

### Triage Tool, Version 2

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Green</th>
<th>Yellow</th>
<th>Red</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Cough</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### UKONS (UK Oncology Nursing Society) Triage Assessment Tool

- Prioritise patients who are symptomatic and who need to be seen urgently.
- Patients with fever, shortness of breath, cough, or diarrhoea should be prioritised.
- Use the tool to assess patients and determine the appropriate level of care.

### Cautions

- Prioritise patients who are symptomatic and who need to be seen urgently.
- Patients with fever, shortness of breath, cough, or diarrhoea should be prioritised.
- Use the tool to assess patients and determine the appropriate level of care.

### Legend

- Green: Not urgent
- Yellow: Urgent
- Red: Critical
<table>
<thead>
<tr>
<th>Reaction</th>
<th>Description</th>
<th>Management</th>
<th>Event</th>
<th>Management</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Is it a new problem? Is it new? How long have you had it? Have you taken any painkillers? Are you allergic to any painkillers?</td>
<td>Moderate pain interfering with daily activities.</td>
<td>Mild pain not interfering with daily activities.</td>
<td>Oral intake altered without significant weight loss or malnutrition.</td>
<td>Oral intake altered in association with significant weight loss or malnutrition.</td>
</tr>
<tr>
<td>Neurosensory/motor</td>
<td>Is there any change in sensation or movement? Is there any change in balance? Are there any visual changes?</td>
<td>Mild sensory loss, weakness, or difficulty with coordination.</td>
<td>No significant decrease in motor function.</td>
<td>Moderate cognitive disability with impaired coordination and activities of daily living.</td>
<td>Severe cognitive disability and/or severe difficulty with coordination and impaired activities of daily living.</td>
</tr>
<tr>
<td>Confusional/cognitive disturbance</td>
<td>Is there a new symptom? Have you had this symptom before? Is it constant?</td>
<td>Severe levels of agitation.</td>
<td>Moderate levels of agitation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>Is this a new problem? Is it getting worse? Is it fatigue?</td>
<td>Severe levels of fatigue.</td>
<td>Mild levels of fatigue.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>Is it itchy or scaly or generalized? Is it rash? Are you feeling generally unwell? Any signs of infection?</td>
<td>Moderate to severe difficulty with coordination and impaired activities of daily living.</td>
<td></td>
<td>Moderate to severe difficulty with coordination and impaired activities of daily living.</td>
<td></td>
</tr>
<tr>
<td>Palmar Plantar syndrome</td>
<td>If you have a specific pathophysiology or if you are taking specific medications.</td>
<td>Painful redness and/or swelling of hands and/or feet with or without pain or redness.</td>
<td>Moderate desquamation, blistering and severe pain.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extravascular</td>
<td>Any problems after administration of treatment? When did the problem start? Is the problem around or along the injection site? Has the patient got a viral illness? Does the problem persist?</td>
<td></td>
<td>Venous or drug related.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTES:**
- Treatment of pain and symptoms should be guided by local guidelines and the patient's individual needs.
- Allergic reactions should be managed according to local guidelines.
- All patients should be advised to seek medical advice if they experience any of the symptoms listed.
- In case of severe symptoms, patients should contact their healthcare provider immediately.

**Reference:**
- Issue Date: 11th September 2020
- Author: Alex Howard & Lauren Williams
- Authorised by: Drug & Therapeutics Committee
- Copy No.: 1

**THE CLATTERBRIDGE CANCER CENTRE NHS FOUNDATION TRUST**

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**Ref. #:**
# Appendix D – Risk Assessment of NICE Guideline CG151

## Risk Assessment Form

<table>
<thead>
<tr>
<th>Dept: Trustwide</th>
<th>Assessment date: 03 May 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead Assessor/s: Joanne McCaughey</td>
<td>Who/What is at risk: Trust reputation</td>
</tr>
</tbody>
</table>

### Risk Information

**Summary of risk (brief description to populate the Trust Risk Register):**

Non compliance with neutropenic sepsis NICE guidance

**Description of risk (background information / detail to give risk context):**

NICE has issued neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients CG151. This guidance has good general principles which would be excellent for implementation within a busy general hospital however as a specialist centre we feel that the guidance is not as comprehensive as the neutropenic policy in existence at CCC at the present. Areas where we feel that it would be inappropriate to introduce to the trust are discussed below:

- **Quinolone prophylaxis.** We do not feel that our patients should be offered a quinolone as prophylaxis for neutropenic sepsis as we feel that the risk of the patients becoming infected with Clostridium difficile is too great in relation to their risk of developing neutropenic sepsis.
- **GCSF.** Patients at high risk of neutropenic sepsis i.e. more than 20% have GCSF funded integral to their regimen.
- **Piperacillin and Tazobactam monotherapy.** Currently patients have their neutropenic sepsis risk assessed using the Multinational Association of Supportive Care in Cancer scoring tool when they are admitted to CCC. They are either designated high or low risk of developing complications. Presently we give IV antibiotics to only the patients at high risk of developing complications and we would prefer to stay with current practice due to the increasing prevalence of ESBL bacteria.
- **Low risk antibiotics.** As we risk assess all our patients we give our low risk patients oral antibiotics. This is a validated method of treating neutropenic sepsis, as a trial was carried out at CCC by Innes HE et al to ensure that oral antimicrobials used for neutropenic sepsis were safe and appropriate in our care setting. This allows us many advantages such as reduced patient stay and reduced cost.

### Existent Control Measures:

(i.e. what is currently in place to reduce the risks)

We have the neutropenic sepsis policy in situ which mandates many of the above points...
**Risk Scoring**

- **Impact score = 3**
- **Likelihood score = 1**

**Risk Score (impact x likelihood) = 3**

A Risk Mitigation Plan must be attached for all risks 15 and over.

**Impact descriptor used (e.g. finance, radiation etc) = Reputation**

<table>
<thead>
<tr>
<th>Action</th>
<th>Responsibility</th>
<th>Due Date</th>
<th>Progress</th>
<th>Completed date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact the individual TSG’s to confirm their position on the use of quinolones as prophylaxis</td>
<td>Dr E Ahmed</td>
<td></td>
<td>Complete</td>
<td></td>
</tr>
<tr>
<td>Prospectively audit neutropenic sepsis patients admitted to CCC, monitoring for ototoxicity and renal toxicity</td>
<td>Dr HE Innes</td>
<td></td>
<td>Complete Feb 14</td>
<td></td>
</tr>
<tr>
<td>Look to site the neutropenic sepsis policy within the acute oncology group rather than in the antimicrobial stewardship. Group does not have suitable quorum at present so will sit with antimicrobial stewardship until appropriate. Microbiology advice is mandatory.</td>
<td>Dr E Ahmed</td>
<td></td>
<td>Complete Feb 14</td>
<td></td>
</tr>
<tr>
<td>Reconvene the antimicrobial stewardship group within two months</td>
<td>Rhiannon Walters-Davies</td>
<td>End of June</td>
<td>Complete</td>
<td></td>
</tr>
</tbody>
</table>

Please send a copy to: the Risk Management Facilitator, CGST
Appendix E – Antimicrobial resources

Aztreonam
BNF link: https://bnf.nice.org.uk/drug/aztreonam.html

Clarithromycin
BNF link: https://bnf.nice.org.uk/drug/clarithromycin.html

Gentamicin
See Appendix F
BNF link: https://bnf.nice.org.uk/drug/gentamicin.html

Meropenem
BNF link: https://bnf.nice.org.uk/drug/meropenem.html

Metronidazole
BNF link: https://bnf.nice.org.uk/drug/metronidazole.html

Tazocin (piperacillin-tazobactam)
BNF link: https://bnf.nice.org.uk/drug/piperacillin-with-tazobactam.html

Teicoplanin
See Appendix G
BNF link: https://bnf.nice.org.uk/drug/teicoplanin.html
Appendix F – Dosing and monitoring guidelines for high-dose gentamicin

Dosing

Exclusion Criteria* (Seek pharmacy advice)

Myasthenia Gravis
Ascites/decompensated liver disease
CrCl <20ml/min
Pregnancy
Major Burns
Endocarditis
Renal replacement therapy
Amputees
Children <16 years old

*Refer to full guideline for further information

1. Initial dose: 5mg/kg (based on actual body weight*) rounded to the nearest 40mg
Use adjusted body weight in obese patients (actual weight >20% of Ideal body weight)

To calculate ideal body weight:
Men = 50kg + 2.3kg every inch over 5 ft
Women = 45.5kg + 2.3kg every inch over 5 ft

To calculate adjusted body weight:
IBW + 0.4 (Actual – ideal)

*Please use clinical judgment and if there is a significant difference between actual and IBW in non-obese patients, decide the dosage based on patient factors and severity of infection

2. Adjust frequency according to gentamicin levels

Please ensure all patients receive a gentamicin leaflet if treatment is to continue for more than 24 hours.

Monitoring

• Obtain a serum concentration level 8-12 hours after the infusion
• Collect a serum gentamicin concentration level using a 7.5ml serum Z tube
• Plot the concentration on the graph below (page 28) to define the recommended dosing frequency
• If the level falls in the area designated Q24h, Q36h or Q48h, the interval should be every 24, 36 or 48 hours respectively. If the level falls on the line choose the longer interval.
• If treatment is to continue monitor trough gentamicin concentration levels twice weekly (more frequent levels may be taken in patients with unstable renal function)
• Aim for a trough level <1mg/l
- Treatment should not be required for more than 7 days. Speak to microbiology if further treatment is needed.

Normogram for gentamicin dosing
## Appendix G – Teicoplanin Therapeutic Drug monitoring

<table>
<thead>
<tr>
<th>Drug and prescribing information</th>
<th>Sampling information and target levels</th>
<th>Factors affecting levels / toxicity</th>
<th>Signs of toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose for all indications:</strong> 12mg/kg</td>
<td><strong>Volume of blood:</strong> Fill to the line</td>
<td><strong>Drug interactions:</strong> Teicoplanin should be used with care in conjunction with other drugs known to be nephrotoxic or ototoxic.</td>
<td><strong>Infusion related toxicities:</strong> In rare cases (even at the first dose), red man syndrome has been observed.</td>
</tr>
<tr>
<td><em>(All doses should be rounded to the nearest 200mg)</em></td>
<td><strong>Tube to use:</strong> Ochre top</td>
<td><strong>Renal function:</strong> Adjustment only required for maintenance doses on day THREE of treatment</td>
<td>Stopping or slowing the infusion may result in cessation of these reactions.</td>
</tr>
<tr>
<td>N.B. In patients who are &gt;100kg, discuss dosing with Pharmacy during working hours (dosing remains as 12mg/kg up to a maximum of 2g per single dose).</td>
<td><strong>Lab performing assay:</strong> Liverpool University Foundation Hospital Trusts</td>
<td><strong>Nephrotoxicity &amp; Ototoxicity:</strong> Patients with renal insufficiency, and/or in conjunction with nephrotoxic drugs (aminoglycosides, colistin, amphotericin B, ciclosporin, and cisplatin) should be carefully monitored, and should include auditory tests.</td>
<td></td>
</tr>
<tr>
<td><strong>Loading dose (regardless of renal function):</strong> 12mg/kg BD for TWO days</td>
<td><strong>Emergency service:</strong> No</td>
<td><strong>Thrombocytopenia:</strong> There is evidence to suggest it is more likely to occur in concentrations &gt;60mg/l but haematological examinations are recommended throughout treatment.</td>
<td></td>
</tr>
<tr>
<td><em>A minimum of 4 doses required for loading</em></td>
<td><strong>Sampling time:</strong> Sampling only required if treatment is to continue &gt;7 days.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maintenance dose (as per renal function):</strong> 12mg/kg ONCE daily from day THREE of treatment</td>
<td><strong>First pre dose trough level to be taken on day 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal dosing (not according to SPC):</td>
<td><strong>Resampling:</strong> Weekly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &gt;60ml/min : 12mg/kg ONCE daily</td>
<td><strong>May be required more frequently if unstable renal function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR 30-60ml/min: 6mg/kg ONCE daily</td>
<td><strong>Target concentration:</strong> Pre dose trough levels should always be below 60mg/l and then as below dependant on indication.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &lt;30ml/min: 4mg/kg ONCE daily</td>
<td>Skin and soft tissue, pneumonia, urinary tract infections: &gt;15mg/l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis: dose as in eGFR &lt;30ml/min</td>
<td>Bone and joint infections: &gt;20mg/l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemodialysis: 12mg/kg THREE times a WEEK. To be given after dialysis.</td>
<td>Sepsis and infective endocarditis: &gt;30mg/l</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>