NEUTROPENIC SEPSIS:
PREVENTION AND MANAGEMENT OF
NEUTROPENIC SEPSIS IN CANCER PATIENTS AT
VELINDRE CANCER CENTRE

This information is issued by the Medicines Management Committee on
the understanding that it is the best available from the resources at our
disposal at the time of preparation

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AUTHOR: Neutropenic sepsis policy working group

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Neutropenic sepsis policy working group
Jaimie Leightfield (Antimicrobial pharmacist)
Brendan Healy (Consultant microbiologist)
Hiliary Williams (Consultant oncologist)
Rosie Roberts (Chemotherapy specialist nurse)
Ceri Stubbs (Clinical lead intensive care)
Ailsa Hayes (Advanced nurse clinician)
# Neutropenic Sepsis Policy

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### 1.1 EXECUTIVE SUMMARY

<table>
<thead>
<tr>
<th>Overview</th>
<th>This document gives guidance on the prevention and treatment of neutropenic sepsis. This document has been updated to incorporate the NICE neutropenic sepsis guidelines.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who</td>
<td>This policy is intended for All Velindre Cancer Centre (VCC) staff.</td>
</tr>
<tr>
<td>Key messages</td>
<td>These guidelines refer to the prevention and treatment of neutropenic sepsis.</td>
</tr>
<tr>
<td></td>
<td>Patients who are <strong>NOT</strong> neutropenic (Neutrophil count &gt; 0.5 x 10^9) must be treated according to the Antimicrobial Policy.</td>
</tr>
<tr>
<td></td>
<td>Patient education is essential and must not be seen as a one off event. All staff should take every opportunity to remind patients and their relatives of the importance of reporting significant symptoms of infection.</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis against neutropenic sepsis with Granulocyte Colony Stimulating Factor (GCSF) or antibiotics must be prescribed in accordance with this policy. Additional prophylaxis outside standard practice must be carefully considered on an individual patient taking into account the advantages, disadvantages and alternatives (e.g. dose reduction or delay).</td>
</tr>
<tr>
<td></td>
<td>Patients who develop symptoms and signs of neutropenic sepsis in the community must contact the chemotherapy pager for triage assessment and then admission to VCC or referral to their local district general hospital if more appropriate.</td>
</tr>
<tr>
<td></td>
<td>Antibiotic treatment must be started within <strong>ONE HOUR</strong> of admission to VCC for all patients with suspected neutropenic sepsis. <strong>DO NOT</strong> wait for Full Blood Count (FBC) or other investigations to be reported.</td>
</tr>
<tr>
<td></td>
<td>Use the Sepsis / Severe Sepsis Screening tool and Sepsis Six pathway for unstable patients. Use the Multinational Association for Supportive Care in Cancer (MASCC) score for stable patients.</td>
</tr>
<tr>
<td></td>
<td>Patients who are not neutropenic but are diagnosed with sepsis should be treated in accordance with this policy.</td>
</tr>
<tr>
<td></td>
<td>Meropenem 1g TDS is first line intravenous (IV) agent. Co-amoxiclav 625mg TDS and Ciprofloxacin 750mg BD are the first line oral (PO) agents.</td>
</tr>
<tr>
<td></td>
<td>All patients categorised as low risk should be assessed using the early discharge criteria on page 18.</td>
</tr>
<tr>
<td></td>
<td>GCSF is <strong>NOT</strong> routinely recommended for the treatment of neutropenic sepsis.</td>
</tr>
<tr>
<td></td>
<td>Guidelines for critical care referral see page 20.</td>
</tr>
<tr>
<td></td>
<td>Dosage and monitoring information for the drugs included in the policy, including renal impairment, see Appendix 1.</td>
</tr>
</tbody>
</table>
2.1 INTRODUCTION

Neutropenic sepsis can be a fatal complication of cytotoxic chemotherapy resulting in hospital admissions, treatment delays and dose reductions. A small number of patients will develop life threatening sepsis as a result of neutropenia, and a mortality rate of approximately 5% has been reported in patients with solid tumours. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD); Systemic anti-cancer therapy: for better for worse? and the National Chemotherapy Advisory Group (NCAG); Chemotherapy service in England; ensuring quality and safety highlighted problems in the management of neutropenic sepsis in adults receiving cytotoxic chemotherapy. These reports recommend the need to develop systems for urgent assessment and organisation level policies for the management of neutropenic sepsis. This policy has been updated in response to the NICE neutropenic sepsis: Prevention and management of neutropenic sepsis in cancer patients guidelines that were published in September 2012.

2.2 DEFINITIONS

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>Neutrophil count ≤ 0.5 x 10^9/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenic sepsis</td>
<td>Neutrophil count ≤ 0.5 x 10^9/L and either clinical signs of infection or a temperature ≥ 38°C.</td>
</tr>
<tr>
<td>MASCC risk index</td>
<td>Multinational association for Supportive Care in Cancer Scoring system for the proposed risk index for identifying low-risk neutropenic sepsis patients.</td>
</tr>
</tbody>
</table>

2.3 CONTACT INFORMATION

Microbiology at UHW .......................................................... via switch

Jaimie Leighfield, Antimicrobial Pharmacist, VCC......................Ext 6223

Gail Lusardi, Lead Infection Prevention and Control Nurse,VCC..Ext 6310

Chemotherapy pager, VCC......................................................Bleep 194
2.4 RESPONSIBILITIES

Antimicrobial Stewardship Group
- Educate staff about how to use and implement policy.
- Audit policy annually to ensure standards are upheld.

Chemotherapy nurses
- Ensure patients are educated about the signs and symptoms of neutropenic sepsis.
- Ensure patients receive the appropriate systemic anticancer treatment leaflet.
- Advise patients when to contact the chemotherapy pager.
- Advise patients about temperature monitoring.

Chemotherapy pager nurses
- Ensure patients are triaged appropriately when they call the chemotherapy pager.
- Follow the guidance within this policy.
- Refer to the patient’s consultant or on-call medical team for advice when appropriate.

Chemotherapy prescribers
- Ensure all patients are educated about how to monitor for signs and symptoms of neutropenic sepsis and what to do if these occur.

Consultants
- Ensure all patients admitted with neutropenic sepsis are reviewed by a consultant and provide support and mentorship to ward medical staff
- Follow guidance within this policy.
- Embrace prudent antimicrobial prescribing and lead practice.

Medical ward staff
- Ensure patients are reviewed promptly and, if appropriate, started on antibiotics within 1 hour of admission.
- Ensure that the severe sepsis screening tool and MASCC risk index are used appropriately to optimise patient treatment.
- Guide appropriate taking of samples for culture.
- Undertake prudent prescribing of antimicrobials.

Ward Nurses
- Ensure patients with suspected neutropenic sepsis have their antibiotics started within one hour.
- Ensure patients have their blood cultures taken before antibiotics are given.
- Ensure that observations are carried out as directed.
- Ensure that therapeutic drug monitoring is undertaken when necessary.

Pharmacists
- Ensure patients receive comprehensive pharmaceutical care.
- Ensure antimicrobials prescribed are appropriate.
- Ensure that therapeutic drug monitoring is undertaken when necessary.
- Ensure patients are educated about the use of antimicrobials.
3.1 PATIENT EDUCATION

Most patients are likely to be in the community when they become neutropenic. Patient education is essential to ensure that they are fully informed of the risk of developing potentially life threatening infections. This must be explained clearly, in terms the patient can understand. Verbal explanations should be backed up by written information before gaining written consent. With the patient’s agreement, wherever possible this information should also be shared with significant relatives or friends identified by the patient. Education is not a one off event and testing patients’ understanding of the information is vital. This can be done by rehearsing with the patient what they would do if they developed one of the key symptoms.

In order to ensure that any signs of infection are detected and treated promptly it is important that patients:

- Have the 24 hour contact number for the chemotherapy pager
- Are aware of key symptoms to report (see below)
- Are able to monitor their temperature at home

All patients are given a yellow chemotherapy alert card (see below) to guide them when to contact the chemotherapy pager.

**You must contact Velindre Cancer Centre immediately any time day or night if you have:**

- a temperature of 37.5 °C or above
- flu like symptoms, chesty cough or any other signs of infection
- shivering episodes
- unusual bruising or bleeding
- vomiting more than once in 24 hours
- four or more bowel movements above normal, or 4 episodes of diarrhoea in 24 hours
- mouth ulcers or soreness that stops you eating or drinking
- been admitted to another hospital for any reason

Patients should be given advice about how to reduce their risk of developing infections. This will include avoiding contact with anyone with obvious signs of infection, maintaining good personal hygiene and having flu vaccinations when available.

Safeguarding of vulnerable adults and patients with any cognitive impairment must be considered when giving education. For more information regarding patients with cognitive impairment please contact Claire Illari, supportive care nurse for dementia and cognition. For more information regarding the safeguarding of vulnerable adults please contact Debbie Bainbridge, patient safety co-ordinator. There is also more information available via the VCC Intranet page.
4.1 PREVENTION OF NEUTROPENIC SEPSIS

Prior to commencing chemotherapy, careful assessment should be carried out to identify patients at risk of developing neutropenic sepsis. The risk of developing neutropenic sepsis is related to both individual patient factors and the chemotherapy prescribed.

Primary prophylaxis is not recommended routinely for previously untreated patients receiving chemotherapy except as part of a clinical trial.

Patients who are at high risk of neutropenic sepsis (neutrophil count ≤0.5×10^9/L) as a consequence of chemotherapy should be offered primary prophylaxis with either antibiotics or Granulocyte Colony Stimulating Factor (GCSF). The regimens in table 1 are classified as high risk (>20% risk of neutropenic sepsis) and have primary prophylaxis with either antibiotics or GCSF automatically added to the electronic prescription.

Where maintenance of dose intensity and dose density is not crucial, treatment delays, dose reduction or use of less myelosuppressive chemotherapy should be considered.

Secondary prophylaxis is preventative treatment for a patient who has already suffered an episode of neutropenic sepsis or very prolonged neutropenia in the absence of fever. GCSF or antibiotics may be considered in situations where dose reductions or delays may be associated with a poor prognosis. Dose reduction may be more appropriate where protracted neutropenia is due to pharmacokinetic factors such as reduced renal or hepatic function.

Individual risk factors for chemotherapy induced neutropenic sepsis (ASCO, 2006)

- Age >65 years
- Poor performance status
- Previous episodes of febrile neutropenia
- Combined chemo-radiotherapy
- Poor nutritional status
- Advanced disease
- Serious co-morbidities
- Open wounds or active infections
- Female
- Haemoglobin <120g/L

Other factors to be considered

- Intent of treatment – Is maintenance of dose intensity crucial?
- Risk associated with chemotherapy regimen – Primary prophylaxis is indicated for regimens with neutropenic sepsis risk >20%.
- For regimens with neutropenic sepsis risk 10-20% consider patient related factors.
- Where dose reductions or delays are known to be associated with poor prognosis (e.g. Adjuvant treatment, potentially curative treatment and when the treatment intent is to prolong survival)

See appendix 6 for risk of neutropenic sepsis associated with common regimens.
### Table 1: Summary of prophylaxis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Prophylaxis</th>
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<tr>
<td>BEP (Bleomycin/Etoposide/Cisplatin)</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7</td>
</tr>
<tr>
<td>Cisplatin/Doxorubicin</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7</td>
</tr>
<tr>
<td>Cisplatin/Etoposide</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7. Cycle 1 only.</td>
</tr>
<tr>
<td>R-DHAP (Rituximab, Ciplatin, Cytrabine)</td>
<td>Filgrastim 30 million units (&lt; 60 Kg) or 48 million units (&gt;60 Kg) from day 6 to 13 (8 days)</td>
</tr>
<tr>
<td>FEC/T 100 (Epirubicin, Flurouracil, Cyclophosphamide or Docetaxel)</td>
<td>Pegfilgrastim 6mg s/c STAT, 24 hours post chemotherapy</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>Co-trimoxazole for duration of treatment and for 6 months after</td>
</tr>
<tr>
<td>IAD (Doxorubicin/ifosfamide)</td>
<td>Ciprofloxacin 500mg BD for 7 days Starting on day 7</td>
</tr>
<tr>
<td>IGEV (Ifosphamide, Gemcitabine, Vinorelbine)</td>
<td>Filgrastim 48 million units OD from days 7 to 12 (6 days) – except for cycles preceding stem cell collection.</td>
</tr>
<tr>
<td>Liposomal daunorubicin (DaunoXome™)</td>
<td>Co-trimoxazole</td>
</tr>
<tr>
<td></td>
<td>Duration of treatment</td>
</tr>
<tr>
<td></td>
<td>Azithromycin 1250mg ONCE a week</td>
</tr>
<tr>
<td></td>
<td>Fluconazole 50mg OD</td>
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<tr>
<td></td>
<td>Aciclovir 400mg QDS</td>
</tr>
<tr>
<td>Pemetrexed/Cisplatin</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7</td>
</tr>
<tr>
<td>R-CHOP 14 (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine)</td>
<td>Filgrastim 30 million units (&lt; 60 Kg) or 48 million units (&gt;60 Kg) from day 6 to 12 (9 days)</td>
</tr>
<tr>
<td>Topotecan</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7</td>
</tr>
<tr>
<td>TPF (Docetaxel/Cisplatin/5FU)</td>
<td>Pegfilgrastim 6mg s/c STAT 24 hours post chemotherapy</td>
</tr>
<tr>
<td>VIDE (Vincristine/ifosfamide/ Doxorubicin/Etoposide)</td>
<td>Ciprofloxacin 500mg BD for 7 days, starting on day 7</td>
</tr>
<tr>
<td></td>
<td>Co-trimoxazole</td>
</tr>
<tr>
<td>Total Body Irradiation with Cyclophosphamide prior to Stem Cell Harvest</td>
<td>Refer to UHW guidelines</td>
</tr>
</tbody>
</table>

*Co-trimoxazole doses vary depending on regimen, please refer to chemocare for doses*
4.2 PROPHYLAXIS WITH GCSF

GCSF stimulates the proliferation, maturation and release of neutrophils resulting in an increase in the number of circulating neutrophils.\textsuperscript{6,7}

\textbf{Pegfilgrastim} - combines filgrastim with a polyethyleneglycol (PEG) molecule resulting in a larger molecule with a reduced renal clearance and longer duration of action. Pegfilgrastim is cleared by neutrophils: it’s serum levels remain high whilst neutrophil levels are low, resulting in a self-regulated clearance mechanism.\textsuperscript{6}

- Dose is 6mg administered as a STAT subcutaneous injection.
- Dose should \textbf{not be} administered less than 24 hours following cytotoxic chemotherapy.
- Pegfilgrastim should \textbf{not be} used for multiple day regimens where chemotherapy is given less than 14 days apart e.g. not suitable for use after Day 1 when chemotherapy is given on Day 8.\textsuperscript{8}

\textbf{Filgrastim} - should be the GCSF of choice for multiple day regimens.

- Dose is 0.5 million-units/kg administered by subcutaneous injection once daily.\textsuperscript{7}
- Dose should \textbf{not be} administered less than 24 hours following cytotoxic chemotherapy.
- Available as 30 million-unit (300 micrograms) and 48 million-unit (480 micrograms) pre-filled syringes. Doses should be rounded to the nearest pre-filled syringe.

4.3 ANTIMICROBIAL PROPHYLAXIS

The risk of infections may be reduced by using prophylactic antibiotics chosen to cover the most likely pathogens and the time period of greatest risk of infection. The most serious bacterial infections are likely to arise from gram negative organisms, but as the degree of immunocompromise increases, significant infections can arise from other organisms.\textsuperscript{4}

The NICE guidelines recommend prophylaxis with a fluoroquinolone during the expected period of neutropenia for adult chemotherapy patients with acute leukaemia, stem cell transplants or solid tumours where significant neutropenia (neutrophil count \textless 0.5x10\textsuperscript{9}/L) is anticipated. It was decided by the VCC neutropenic sepsis policy working group that we would continue to use a combination of GCSF or antibiotics in accordance with this policy. Ciprofloxacin can cause diarrhoea, vomiting or allergic reactions. There are also concerns that prophylactic use of antibiotics may lead to antibiotic resistance in the local community.\textsuperscript{4} Prophylaxis with antibiotics should only be prescribed in accordance with this policy and for the shortest period possible. All other cases should be discussed with microbiology. Where ciprofloxacin is not considered appropriate please contact the antimicrobial pharmacist or microbiology for advice.

Co-trimoxazole is recommended for prophylaxis of \textit{Pneumocystis jiroveci} (PJP). The dose varies depending on the regimen, please check chemocare for dose.
5.1 TRIAGE ASSESSMENT

Chemotherapy pager:

Patients have access to 24 hour advice from an experienced oncology nurse of band 6 or above carrying a pager. The patient will be assessed using the guidelines in appendix 2 and 3. Where any doubt exists about whether the symptoms reported are significant this will be discussed with the patient’s medical team or if unavailable the on call medical team.

Admission to Velindre Cancer Centre with suspected infective neutropenia

Any patient with suspected neutropenic sepsis must be brought into hospital for urgent clinical assessment. This may be to any inpatient area at Velindre or at a local hospital.

Assessment /admission to a local hospital must be arranged if no beds are available at Velindre, or if it is felt to be more appropriate due to the distance from Velindre or if the patient’s clinical condition warrants local admission (see Appendix 5)

- If possible the patient should be admitted to a cubicle, however prompt assessment and treatment is a higher priority than isolation in reducing adverse patient outcomes.
- The patient should be assessed promptly using the suspected neutropenic sepsis proforma. See page 11 for full history and examination criteria.
- The doctor admitting the patient should inform the patient’s consultant that their patient has been admitted.
5.2 HISTORY AND EXAMINATION

Use the suspected neutropenic sepsis admission proforma (appendix 6) and ensure that all patients are seen by a doctor and have the appropriate antibiotics started within ONE HOUR of admission. The same principles apply if a patient who is already an in-patient at VCC develops signs of sepsis.

A detailed history should be taken including:

- Onset of fever/ rigors
- Fever/ rigors related to line flushing
- Any recent blood products
- Nature of chemotherapy given
- Prior prophylactic antibiotics
- Concomitant steroid use – can mask signs and symptoms of infection
- Recent surgical procedure
- Presence of allergies – may dictate choice of antibiotic therapy

Check clinical records for past positive microbiology results for recent cultures and sensitivities (e.g. antibiotic resistant organisms or recent bacteraemia). Always complete careful examination and systems review for potential foci of infection (important as some infections e.g. community acquired pneumonia, may not be covered by empirical antibiotics chosen for treating neutropenic sepsis.)

- Eyes (including fundi)
- Mouth, gums, teeth and mucosa
- Upper GI symptoms
- Abdominal pain or Distension
- Vascular access site
- Genito-urinary tract discharge of dysuria
- Ears, nose and throat
- Respiratory – SOB, cough and sputum
- Skin – consider fungal, herpes zoster and pseudomonas
- Perineum – especially anus
- Diarrhoea – always consider C.difficile
5.3 INITIAL MANAGEMENT OF NEUTROPENIC SEPSIS

Patients may initially look well but a small number can rapidly develop septic shock. All patients with suspected neutropenic sepsis should be reviewed by a doctor and have antibiotics started within ONE HOUR of admission. Use the suspected neutropenic sepsis admission proforma when admitting patients.

Patients who are already In-patients at VCC must be assessed promptly using the same assessment and treatment criteria.

**Record baseline observations**
- Temperature, Pulse, Blood Pressure, Respirations, O₂ saturations, Level of consciousness (use AVPU – Alert, Verbal, Pain, Unresponsive)
- Repeat observations at least 3 times at 15 minute intervals and calculate the NEWS score. Monitor urine output and start a fluid balance chart.

**Initiate Investigations - All patients** – FBC, RLB, CRP, Blood culture (peripheral and central), BM, Lactate and MSU.
**If indicated** – Sputum, Stool sample, Wound swab, CXR

**Use Sepsis / Severe sepsis screening tool**
- Admit and start IV Meropenem 1g TDS or Vancomycin 1g BD and Gentamicin 6mg/kg OD for penicillin allergy
- DO NOT WAIT FOR FBC – Antibiotics must be started within ONE hour of admission
- Use Sepsis/Severe Sepsis Screening tool (page 13) to assess need for Sepsis Six care pathway (page 14)

**Use MASCC risk index**
- Admit and calculate MASCC score using table on page 15
- Use flow chart on page 16 to determine treatment.

**DO NOT WAIT FOR FBC – Antibiotics must be started within ONE hour of admission**
- If you have any concerns start IV antibiotics and use Sepsis/Severe Sepsis Screening tool (page 13)

*NEWS*= National Early Warning Score. For actions – see Appendix 9
**MASCC**= Multinational Association for Supportive Care in Cancer (Page 15)
5.4 SEPSIS / SEVERE SEPSIS SCREENING TOOL

This screening tool should be used to assess all patients who are clinically unwell, causing concern or have a NEWS score ≥ 3 to determine whether they require the Sepsis Six severe sepsis care pathway. Elements of this tool are included in the suspected neutropenic sepsis admission proforma, however this tool can still be used for all patients, especially for In-patients who develop signs and symptoms of sepsis. Full size copies can be found on all wards and if used they should be filed in the patients notes on discharge.

Are any 2 of the following Signs/symptoms of Infection criteria present and new to your patient?
- Temperature <36 or >38.6 °C
- Heart rate >90bmp
- WCC >12 or < 4 x 10⁹/L
- Respiratory rate >20/min
- Acutely altered mental state
- Hyperglycaemia in the absence of diabetes
- Neutrophils <0.5 x 10⁹/L

If NO, treat for sepsis:
- Oxygen therapy as necessary
- Blood cultures
- Antibiotics (oral or IV)
- Fluid therapy as necessary
- Reassess for SEVERE SEPSIS with 2-4 hourly observations or as clinically indicated

If YES, patient has severe sepsis
Start SEVERE SEPSIS CARE PATHWAY
i.e. SEPSIS SIX

Are there any signs of NEW organ dysfunction?
- SBP < 90mmHg or MAP < 65mmHg
- Urine output < 0.5ml/kg/hr for 2 hrs
- INR > 1.5 or APTT > 60s
- Bilirubin > 34 µmol/I
- Lactate > 2 mmol/I
- New need for oxygen to keep SpO₂ > 90%
- Platelets < 100 x 10⁹/L
- Creatinine > 177 µmol/I

If NO, treat for sepsis
- Oxygen therapy as necessary
- Blood cultures
- Antibiotics (oral or IV)
- Fluid therapy as necessary
- Reassess for SEVERE SEPSIS with 2-4 hourly observations or as clinically indicated

If YES, patient has Signs and Symptoms of infection / Systemic Inflammatory Response Syndrome

Does your patient have a history or signs suggestive of a new infection?
- Cough/ sputum/ chest pain
- Abdo pain/ distension/ diarrhoea
- Line infection
- Endocarditis
- Dysuria
- Headache with neck stiffness
- Cellulitis/ wound infection/ septic arthritis
- New need for oxygen to keep SpO₂ > 90%
- Platelets < 100 x 10⁹/L
- Creatinine > 177 µmol/I

If YES, patient has sepsis
- Heart rate >90bpm
- WCC >12 or < 4 x 10⁹/L
- Temperature <36 or >38.0°C

If YES but patient meets the criteria within shaded boxes and has received chemotherapy within the last 3 weeks treat as NEUTROPENIC SEPSIS

Dysuria
Headache with neck stiffness
Cellulitis/ wound infection/ septic arthritis
If YES, patient has Signs and Symptoms of infection / Systemic Inflammatory Response Syndrome
5.5 SEPSIS SIX SEVERE SEPSIS CARE PATHWAY

This care pathway should be used to assess all patients who have been identified as having severe sepsis. This tool should be used for all patients, especially for In-patients who develop signs and symptoms of sepsis. Full size copies can be found on all wards and if used they should be filed in the patients notes on discharge. Referral to critical care should also be considered, see page 18 for more information.

[Severe Sepsis Care Pathway image]
5.4 MASCC RISK ASSESSMENT

The Multinational Association for Supportive Care in Cancer (MASCC) risk index is an assessment tool which has been validated for use in cancer patients. It has been endorsed by ESMO in their guidelines for Management of Febrile Neutropenia: ESMO Clinical Practice Guidelines and the NICE Neutropenic sepsis: prevention and management of patients with neutropenic sepsis guidelines.

Table 2 below shows the MASCC risk index which is used to differentiate between high risk and low risk patients who have already been identified as stable. If you have any concern about a patient follow the unstable patient pathway and use the severe sepsis screening tool.

### Table 2 – MASCC risk index

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>≥ 60 years</td>
<td>0</td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>2</td>
</tr>
<tr>
<td><strong>Patient dehydrated, requiring fluids?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td><strong>Patient systolic blood pressure</strong></td>
<td></td>
</tr>
<tr>
<td>Systolic BP &lt;90mmHg</td>
<td>0</td>
</tr>
<tr>
<td>Systolic BP ≥90mmHg</td>
<td>5</td>
</tr>
<tr>
<td><strong>Does the patient have COPD?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
</tr>
<tr>
<td><strong>Does the patient have a solid tumour or no previous fungal infection in a haematological malignancy?</strong></td>
<td>4</td>
</tr>
<tr>
<td>Solid tumour or no previous fungal infection in a haematological malignancy</td>
<td></td>
</tr>
<tr>
<td>Haematological malignancy with previous fungal infection</td>
<td>0</td>
</tr>
<tr>
<td><strong>Does the patient have symptoms related to this infective neutropenic episode?</strong></td>
<td></td>
</tr>
<tr>
<td>None or mild symptoms</td>
<td>5</td>
</tr>
<tr>
<td>Moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Severe symptoms</td>
<td>0</td>
</tr>
<tr>
<td><strong>Was the patient already an inpatient before this episode of infective neutropenia?</strong></td>
<td></td>
</tr>
<tr>
<td>Admitted with this episode</td>
<td>3</td>
</tr>
<tr>
<td>Already an inpatient</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: scoring attributed to ‘symptoms related to this episode of neutropenic sepsis and is not cumulative, therefore the maximal theoretical score is 26

Patients with a score of < 21 = HIGH RISK of complications (consider IV antibiotic therapy)

Patients with a score of ≥ 21 = LOW RISK of complication (consider oral antibiotic therapy)
5.5 TREATMENT PATHWAY FOR PATIENTS ASSESSED USING MASCC RISK INDEX

**HIGH RISK PATIENTS (MASCC <21)**

Admit and start IV Meropenem 1g TDS. DO NOT WAIT FOR FBC
(Gentamicin 6mg/kg OD and Vancomycin 1g BD\(^1\) for patients with anaphylactic penicillin allergy)
Vanc dose should be reduced to 750mg BD for patients < 60Kg see page 27)

Is the neutrophil count ≤0.5 x 10^9?

- YES
  - Review the patient daily
  - Is the patient clinically stable, symptomatically better, and is there evidence of fever lysis?
    - Reducing CRP
    - Afebrile
    - Rising white cell and Neutrophil count
  - If YES, continue with treatment as per antimicrobial policy.
  - If NO, consider switching to oral Co-amoxiclav 625mg TDS and Ciprofloxacin 750mg BD.
    - (levofloxacin 500mg BD for penicillin allergy)
    - OR oral antibiotics indicated from MC+S

Is the patient suitable for early discharge? (Early discharge criteria on page 19)

- YES
  - Discharge patient with 7 day course (in total) of oral antibiotics.
    - Co-amoxiclav 625mg TDS and ciprofloxacin 750mg BD (levofloxacin 500mg BD for penicillin allergy)
    - OR oral antibiotics indicated from MC+S
- NO
  - Review the patient daily and check for any microbiological cultures and sensitivities.
    - Amend treatment accordingly and use oral antibiotics where appropriate.
  - Is the patient clinically stable and symptomatically better?
    - YES
      - Discharge patient
    - NO

**LOW RISK PATIENTS (MASCC≥21)**

Admit patient and start oral Co-amoxiclav 625mg tds and ciprofloxacin 750mg bd for 7 days. (levofloxacin 500mg bd for penicillin allergy)

Is the neutrophil count ≤0.5 x 10^9?

- YES
  - Treat as per antimicrobial policy
- NO
  - Admit patient for a minimum of 24 hours and start PO Co-amoxiclav 625mg TDS and Ciprofloxacin 750mg BD.
    - (Levofloxacin 500mg BD for penicillin allergy)
  - Is the patient suitable for early discharge? (Early discharge criteria on page 19)
    - YES
      - Discharge patient
    - NO
  - Review the patient daily and check for any microbiological cultures and sensitivities.
    - Amend treatment accordingly and use oral antibiotics where appropriate.
  - Is the patient clinically stable and symptomatically better?
    - YES
      - Discharge patient
    - NO

\(^1\) Vancomycin 1g BD is recommended for patients with anaphylactic penicillin allergy.
5.6 PRESCRIBING GUIDELINES

<table>
<thead>
<tr>
<th>CLINICALLY UNWELL PATIENTS OR HIGH RISK (MASCC &lt;21)</th>
<th>LOW RISK (MASCC ≥21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meropenem 1g TDS</td>
<td>Ciprofloxacin 750mg bd and Co-amoxiclav 625mg tds for 7 days</td>
</tr>
</tbody>
</table>

- Treatment should be guided by sensitivities reported by microbiology and clinical signs and symptoms.
- Patients with epilepsy should not receive ciprofloxacin or levofloxacin – discuss with microbiology for choice of therapy.
- Patients taking sodium valproate should not receive meropenem – Meropenem reduces the plasma concentration of sodium valproate and increases the risk of seizures. Piperacillin and Tazobactam (Tazocin™) would be a suitable alternative for patients who are not penicillin allergic.

**START with STAT** – the first dose should be prescribed in the STAT medication box on the front of the drug chart and the time administered recorded.

- Antibiotics should be reviewed when the FBC is reported. Not neutropenic (neuts < 5x10⁹/L) → prescribe neutropenic sepsis antibiotics on the main section of the drug chart.

Not neutropenic (neuts > 0.5x10⁹/L) → reviewed antibiotics in accordance with the antimicrobial policy.

Patients who are NOT neutropenic can still be SEPTIC – USE THIS POLICY TO GUIDE TREATMENT OF PATIENT WITH SEPSIS WHO ARE NOT NEUTROPENIC

- The indication and review date/duration for all antimicrobials prescribed must be written in the medical notes.

All patients with neutropenic sepsis/sepsis should be reviewed daily by the ward medical team and discussed at the Acute Oncology Service (AOS) meeting.
5.7 SUSPECTED/PROVEN LINE INFECTION

NICE does not recommend routine use of vancomycin for patients with suspected/proven neutropenic sepsis even if a central or peripheral access line is present.

Vancomycin has a significant side effect profile (e.g. nephrotoxicity and ototoxicity) and the routine addition of vancomycin is likely to do more harm than good.

It is **not** appropriate to add vancomycin for every patient with a fever and a central or peripheral line.

Meropenem is the standard treatment for neutropenic fever in Velindre. It covers most infections with some exceptions; most notably resistant gram positive organisms such as MRSA, *enterococci*, *corynebacterium* and *Coagulase negative staphylococci* (which can all cause line infections). *Coagulase negative staphylococci* (the commonest cause of line infections) tend to cause low grade infections.

In patients with low grade infection it is appropriate to use Meropenem therapy initially and to add vancomycin if a resistant gram positive organism is grown.

Addition of vancomycin may be **considered** in the following scenarios:

- An organism resistant to meropenem is grown (see above and contact microbiology for advice)
- The patient **definitely** has a line infection (good evidence of line infection – redness around line, rigor on flushing etc)
- The patient is very sick (septic shock or severe sepsis) and has a central or peripheral line.
- The patient is known to be colonised with MRSA.

All patients should be reviewed on an individual patient basis, prescriptions reviewed in the light of culture results and cases should be discussed with microbiology if further advice is needed.
5.8 IV to PO SWITCH

All intravenous (IV) antimicrobials should be switched to an oral (PO) equivalent as soon as clinically appropriate. This needs to be weighed up with the risk of switching to oral antibiotics too early and having to convert back, resulting in increased risk of side effects and increased in patient stay.

Review the antibiotics daily on individual patient basis. A switch to oral therapy (or stopping of antimicrobials) should be considered (in patients with no concerns over gastro-intestinal absorption) where there is evidence of clinical improvement such as:

- Resolution of fever for > 24 hours
- Pulse rate < 100 beats/min
- Resolution of hypotension
- Local signs and symptoms improving
- Rising neutrophil and white cell count
- Falling serial CRP measurement
- Clinically hydrated and taking oral fluids

Suggested antimicrobial to oral switch

<table>
<thead>
<tr>
<th>IV</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meropenem 1g TDS for neutropenic sepsis/sepsis</td>
<td>Co-amoxiclav 625mg TDS + Ciprofloxacin 750mg BD</td>
</tr>
<tr>
<td>Gentamicin and Vancomycin for penicillin allergic patients</td>
<td>Levofloxacin 500mg BD</td>
</tr>
<tr>
<td>Vancomycin for line infection</td>
<td>Contact microbiology for advice</td>
</tr>
<tr>
<td>Tazocin 4.5g TDS for patient taking sodium valproate for seizures</td>
<td>Avoid quinolones (ciprofloxacin and levofloxacin) – contact microbiology for advice</td>
</tr>
</tbody>
</table>

- Treatment should be guided by sensitivities reported by microbiology and clinical signs and symptoms.
- Please see antimicrobial guidelines for full IV to PO switch policy.
- **Patients with epilepsy should not receive ciprofloxacin or levofloxacin** – discuss with microbiology for choice of therapy.
- **Patients taking sodium valproate should not receive meropenem** – Meropenem reduces the plasma concentration of sodium valproate and increases the risk of seizures. Piperacillin and Tazobactam (Tazocin™) would be a suitable alternative for patients who are not penicillin allergic, discuss oral treatment with microbiology,
5.9 PENICILLIN ALLERGY

There is a possibility of cross sensitivity reactions in patients receiving meropenem who are allergic to penicillin. Patients who have anaphylaxis (type 1 reaction) when exposed to penicillin are most at risk and meropenem should be avoided in these patients. The characteristics of a type 1 reaction are:

- Onset of rash within first 72 hours
- Urticaria
- Local swelling
- Itchy rash at any time (even if > 72 hours)
- Laryngeal oedema
- Bronchospasm
- Hypotension

Patients who report side effects such as nausea, vomiting and diarrhoea should not be classified as penicillin allergic and can receive meropenem (and other beta lactam agents). Patients with non type 1 reactions to penicillin can normally receive meropenem (weigh benefit against risk).

5.10 ASSESSMENT FOR EARLY DISCHARGE

Neutrophil count \( \leq 0.5 \times 10^9/L \): According to ESMO\(^{13}\) there is evidence to support early discharge in low risk patients after a minimum of 24 hours in hospital. They must be clinically stable, symptomatically better and meet the criteria for early discharge.

Neutrophil count \( > 0.5 \times 10^9/L \): the patient should be assessed and treated for infection as per the antimicrobial guidelines.

Criteria for early discharge

For low risk patients who are clinically stable and symptomatically better, if the following criteria are met you can consider early discharge:

- Does the patient have someone at home to support them?
- Does the patient have access to a telephone?
- Does the patient have access to transport if required?
- Does the patient live within a 30 minute travel time from the hospital?
- Is the patient registered with a GP surgery or health centre?
5.11 TREATMENT OF NEUTROPENIC SEPSIS WITH GCSF

Pegfilgrastim should NOT be used for the routine treatment of neutropenia.

Treatment of neutropenic sepsis with GCSF should be limited to those patients who are not responding to appropriate antibiotic management and who are developing life-threatening infection (such as severe sepsis, septic shock, pneumonia or invasive fungal infection).5,10

Filgrastim

Dose is 0.5 million-units/kg administered by subcutaneous injection, once daily until neutrophil count is in normal range (usually up to 14 days).7

Available as 30 million-unit (300 micrograms) and 48 million-unit (480 micrograms) pre-filled syringes. Doses should be rounded to the nearest pre-filled syringe.7

The first dose should not be administered less than 24 hours following cytotoxic chemotherapy.

Intravenous administration of filgrastim is no longer recommended. The British Committee for Standards in Haematology (BCSH) guidelines for the use of platelet transfusions supports the use of subcutaneous injections in patients with thrombocytopenia.14

Side effects (See individual SPCs for more details)

- Bone pain is very common (>10%) and generally mild to moderate severity, this is transient and may be controlled in most patients with standard analgesics.
- Allergic type reactions
- Mild to moderate elevations in uric acid and alkaline phosphatase
- Splenomegaly (generally asymptomatic) but very rarely splenic rupture
- Pulmonary adverse effects, in particular interstitial pneumonia, have been reported after G-CSF administration
5.12 GUIDELINES FOR CRITICAL CARE REFERRAL

When assessing a patient with neutropenic sepsis who shows any indications of severe sepsis (see below) then a Critical Care referral must be considered. This decision must be made promptly and a referral should be made sooner rather than later. The referral must be made on a Consultant to Consultant basis, however out of hours and in exceptional circumstances only, if this process can be accelerated by a more prompt discussion between the SPR and the Critical Care Consultant then this may be appropriate. This can only be undertaken if the SPR on site has spoken to the Consultant oncologist on call.

If transfer appropriate contact Critical care Consultant via UHW switchboard

<table>
<thead>
<tr>
<th>Indications of severe sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP &lt;90 (or mean arterial pressure &lt;65)</td>
</tr>
<tr>
<td>Urine output &lt;0.5ml/kg/hr for 2 hours</td>
</tr>
<tr>
<td>INR &gt;1.5 or APTT &gt;60s</td>
</tr>
<tr>
<td>Bilirubin &gt;34</td>
</tr>
<tr>
<td>Lactate &gt;2</td>
</tr>
<tr>
<td>New need for O₂ to keep SpO₂ &gt;90%</td>
</tr>
<tr>
<td>Platelets &lt;100</td>
</tr>
<tr>
<td>Creatinine &gt;177</td>
</tr>
</tbody>
</table>

It can be a very difficult decision to determine whether a patient is an ideal candidate for Critical Care intervention.

There are certain patients who are generally suitable, such as:
- Adjuvant chemotherapy
- Curative treatment
- Those responding to first line chemotherapy for chemo-sensitive disease

There are also patients where Critical care intervention would generally be inappropriate:
- Progressive chemo-resistant disease
- Advanced malignancies
- Other significant co-morbidities i.e. severe COPD

Unfortunately there are a group of patients for whom the decision is more difficult. This is where discussions with the family, Consultant and Critical care are important. Although it can be a difficult decision it should be made promptly as admitting patients to Critical Care before there is significant end organ damage can make a significant difference to patient outcome.
6.1 IMMUNISATIONS

Immunosuppressed patients should be given inactivated vaccines in accordance with national recommendations. However, these individuals may not mount as good an antibody response as immunocompetent individuals. Wherever possible, immunisation should be carried out up to 2 weeks before immunosuppression occurs or deferred until after treatment. 17

All patients should be encouraged to receive the seasonal flu vaccine at their GP surgery. For more information regarding seasonal influenza please contact the infection control team.

6.2 POST EXPOSURE TO INFECTIOUS DISEASES

If you suspect a patient has come into contact with an infectious disease you can contact the Microbiology or Virology department at UHW for advice if you have any concerns. There is somebody available from both departments to provide telephone advice 24 hours a day, 7 days a week. Out of hours the service is provided via a non resident on call system. Urgent queries out of hours should be dealt immediately. Non urgent queries should be dealt with during working hours of the next working day.

If the patient has been admitted to VCC and they have been in contact with an infectious disease please isolate the patient, contact Microbiology or Virology department at UHW for advice and inform the infection control team.
REFERENCES


APPENDIX 1
DRUG DOSAGE AND MONITORING INFORMATION

For more information regarding drugs listed below please refer to the individual drug summary of product characteristics: [http://www.medicines.org.uk](http://www.medicines.org.uk) or the BNF.\(^\text{15}\)

For more information regarding dose adjustments regarding doses in renal impairment please refer to a pharmacist. Dose reductions for renal impairment taken from The Renal Drug Handbook 2007.\(^\text{16}\)

<table>
<thead>
<tr>
<th>MEROPENEM</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>1g IV Three times daily</td>
</tr>
<tr>
<td><strong>Caution</strong></td>
<td>Anaphylactic penicillin allergy (page 17)</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Give 1g IV bolus over approximately 5 minutes Reconstitute 1g vial with 20mL of Water for Injection</td>
</tr>
<tr>
<td><strong>Renal impairment</strong></td>
<td><strong>GFR (mL/min)</strong></td>
</tr>
<tr>
<td></td>
<td>20-50</td>
</tr>
<tr>
<td></td>
<td>10-20</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Avoid concomitant use with Sodium Valproate – Contact microbiology for advice.</td>
</tr>
</tbody>
</table>
**VANCOMYCIN**

<table>
<thead>
<tr>
<th>Dose</th>
<th>50kg - 60kg = 750mg</th>
<th>&gt;60kg – 80kg = 1g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients &lt;50kg or &gt;80kg can receive 15mg/kg up to a maximum of 2g. Seek advice from microbiology if using more than 1g dose.</td>
<td>The dose interval should be based on renal function for patients with a stable creatinine. Seek advice from nephrology if renal function unstable.</td>
</tr>
</tbody>
</table>

Use the Cockcroft and Gault equation to calculate Creatinine Clearance.

\[
\text{CrCl} = \frac{(140 - \text{Age}) \times \text{Body weight (Kg)} \times 1.25}{\text{Creatinine (micromols/L)}}
\]

Use the table below to work out the dose interval based on the Creatinine clearance.

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)</th>
<th>&gt; 80</th>
<th>80</th>
<th>60</th>
<th>40</th>
<th>30</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose interval (hours)</td>
<td>12</td>
<td>18</td>
<td>24</td>
<td>36</td>
<td>48</td>
<td>60</td>
</tr>
</tbody>
</table>

Further advice is available from your ward pharmacist.

**Caution**

Infuse slowly – risk of “red man” syndrome. Caution in renal impairment.

**Administration**

Add 750mg to 250mL sodium chloride 0.9% over 100 minutes
Add 1g to 250mL sodium chloride 0.9% over 100 minutes (max rate 10mg/minute)

**Interactions**

Ciclosporin and caution with diuretics.

**Monitoring**

- Take a blood level **IMMEDIATELY** before the morning administration of the 3rd or 4th dose of vancomycin.
- **DO NOT WAIT** for blood levels to be available.
- Check patients GFR or serum creatinine and if within normal limits (GFR/Serum Creatinine result should have been taken within the previous 4 days) administer the next dose immediately.
- The trough level is then used to determine any modifications for the 4th or 5th dose accordingly.
- The target trough level is between **10 to 15mg/L**.
Neutropenic Sepsis Policy

GENTAMICIN

| Dose         | 6mg/Kg ONCE daily (Max dose 600mg)  
              | Patients admitted between Midnight and 09.00 and receive 3mg/kg  
|
| Caution      | Ascites – patients can take longer to eliminate gentamicin than would be predicted by their renal function.  
              | Contra-indicated in patients with myasthenia gravis  
|
| Administration | Infuse over 60 minutes in 50-100ml sodium chloride  
                  | 0.9% or glucose 5%  
                  | Do not flush with heparin  
                  | Do not mix with penicillins or at a Y site with a penicillin  
|
| Renal impairment | GFR (mL/min)  
                  | Dose (avoid if possible in patients with GFR<30mL/min)  
                  | 30-70  
                  | 6mg/Kg ONCE daily  
                  | 10-30  
                  | Seek advice from pharmacist  
                  | <10  
                  | Seek advice from Nephrology +/- Microbiology  
|
| Interactions | Ciclosporin, amphotericin, cisplatin, vancomycin and other nephrotoxic agents – increased risk of nephrotoxicity  

Monitoring

- Take first trough level immediately before second dose.
- 5-10ml of blood must be sent in a plain tube marked "ONCE DAILY GENT". Send it to the lab as soon as possible (although sample can be stored in refrigerator overnight if last transport has gone).
- State the sampling time and time of the last dose on the request form.
- Check patients GFR or Serum Creatinine and if within normal limits, give second dose, do not wait for level to be reported. (GFR/Serum Creatinine should have been taken within the previous 4 days)
- The trough level is then used to determine any modifications for the third dose.
- Contact Pharmacy for advice if GFR below 50ml/min or Serum Creatinine above reference range.
- Trough level should be < 1.0mg/L
### CO-AMOXICLAV

<table>
<thead>
<tr>
<th>Dose</th>
<th>625mg THREE times a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caution</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Administration</td>
<td>Orally or Liquid via NG/PEG</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-50</td>
<td>Oral and IV: dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10-30</td>
<td>IV: 1.2g BD</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Oral: dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV: 1.2g STAT followed by 1.2g BD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral: dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

### CIPROFLOXACIN

<table>
<thead>
<tr>
<th>Dose</th>
<th>750mg TWICE a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caution</td>
<td>Avoid in patients with history of seizures and epilepsy</td>
</tr>
<tr>
<td>Administration</td>
<td>Orally or Liquid via NG/PEG</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>50-100% of normal dose</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50% of normal dose</td>
<td></td>
</tr>
</tbody>
</table>

**Interactions**
Amiodarone, Warfarin, Theophylline. Please seek advice from the pharmacist if necessary.

### LEVOFLOXACIN

<table>
<thead>
<tr>
<th>Dose</th>
<th>500mg TWICE a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caution</td>
<td>Avoid in patients with history of seizures and epilepsy</td>
</tr>
<tr>
<td>Administration</td>
<td>Oral. No liquid available, tablets can be crushed.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-50</td>
<td>Initial dose 250-500mg then dose reduce by 50%</td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>Initial dose 250-500mg then 125mg 12-24 hourly</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose 250-500mg then 125mg 24-48 hourly</td>
<td></td>
</tr>
</tbody>
</table>

**Interactions**
Amiodarone, Warfarin, Theophylline. Please seek advice from the pharmacist if necessary.
APPENDIX 2

Telephone advice for chemotherapy patients with pyrexia of 37.5°C or above

- **Temperature 38°C or above?**
  - **YES**
    - Advise to attend immediately for FBC and review
  - **NO**
    - Temperature 37.5°C – 37.9°C?
      - **YES**
        - Has the patient any of the following:
          - Obvious signs of infection eg productive cough, dysuria
          - Diarrhoea
          - Weakness/giddiness/fainting
          - Unusual bruising or bleeding
          - Rash
          - Central line or wound
          - History of rigors
          - History of previous admission for neutropenic fever
          - Is the patient at/near the nadir point
          - Severe mucositis / oral thrush
      - **NO**
        - **YES**
          - Advise patient to check temperature regularly and to phone if above 37.5°C for 2 consecutive readings more than 2 hours apart, or 38°C or above on one occasion
          - Advise patient to phone if any other symptoms of infection develop
        - **NO**
          - Ask patient to recheck temperature in 2 hours.

*NB: if patient unable to attend Velindre for FBC and review follow the guidelines for referral to another hospital for check FBC and review if appropriate. Senior medical staff must be informed of this decision.*
APPENDIX 3

Telephone advice for chemotherapy patients with signs of infection
with temperature below 37.5°C

Does the patient have any of the following symptoms:
- Weakness/giddiness/fainting
- Uncontrolled diarrhoea
- Unusual bruising or bleeding
- Inflamed wound or central line
- History of rigors

Advise to attend immediately for FBC and review

Is the patient taking paracetamol or anti inflammatory drugs which may mask a temperature?

Advise to recheck temperature when effects of drugs have worn off.
(allow 4 hours)
37.5°C or above when rechecked?

Advise to recheck temperature three times daily while symptomatic
Phone back if temperature rises above 37.5°C or if symptoms worsen
APPENDIX 4

Guidelines for admission of suspected neutropenic patients to other hospitals

If VCC has no beds, or it is felt to be more appropriate for a suspected neutropenic patient to be assessed at a local hospital (e.g. because of distance or clinical condition):

1. Identify nearest acute hospital (must have acute emergency facilities)

   **Velindre Doctor:**
   - Refer promptly to local medical team and bed manager to arrange assessment/admission.
   - Ensure receiving hospital aware of risk of neutropenia and risk of sepsis. Patient must be assessed promptly.
   - Inform nurse with chemo pager/operational pager of where patient is to be seen

   **Chemo pager or operational pager nurse:**
   - Inform patient of place of admission & ensure patient has transport
   - Liaise with staff in receiving hospital to check if they have access to a neutropenia policy – if not arrange to fax a copy
   - Fax a copy of the patients Velindre medical records from CANISC
   - Document on CANISC and leave a message for the consultants team via secretary
   - Ensure follow up call requested

2. Follow up call
   - Establish outcome of assessment – were they neutropenic? admitted or sent home?
   - If neutropenic are they stable and on antibiotics
   - If they are on continuous chemo via pump or oral chemo has it been stopped
   - Ensure staff aware they can contact Velindre anytime for advice
APPENDIX 5

Frequency of neutropenic sepsis associated with Common UK chemotherapy regimens

NB: This list is not exhaustive. Clinical judgment should always be used

Primary prophylaxis is indicated for regimens with neutropenic sepsis risk >20%. For regimens with neutropenic sepsis risk 10-20% consider patient related factors.

<table>
<thead>
<tr>
<th>Tumour site</th>
<th>Regimen</th>
<th>Neutropenic sepsis risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td><strong>FEC100-T</strong>: Fluorouracil 500mg/m², epirubicin 100mg/m², cyclophosphamide 500mg/m², d1 of 21 day cycle for 3 cycles then docetaxel 100mg/m² d1 of 21 day cycle for 3 cycles</td>
<td>25</td>
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<td></td>
<td><strong>FAC</strong>: Fluorouracil 500mg/m², epirubicin 100mg/m², cyclophosphamide 500mg/m², d1 of 21 day cycle for 3 cycles then docetaxel 100mg/m² d1 of 21 day cycle for 3 cycles</td>
<td>4.4</td>
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<tr>
<td>Lung</td>
<td><strong>Carboplatin/Etoposide</strong></td>
<td>10-20</td>
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<td><strong>Gemcitabine/Cisplatin</strong></td>
<td>7</td>
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<td>Colorectal</td>
<td><strong>FOLFIRI</strong>: Either irinotecan 80mg/m², fluorouracil infusion (24h) 2300mg/m², calcium folinate 500mg/m² d1 weekly OR irinotecan 180mg/m², fluorouracil 400mg/m² bolus and 600mg/m² 22 hour infusion and calcium folinate 500mg/m² d1 of 14 day cycle</td>
<td>11</td>
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<td><strong>FOLFOX</strong>: Oxaliplatin 85mg/m² d1, leucovarin 200mg/m², fluorouracil 400mg/m² bolus and 600mg/m² 22 hour infusion d1 and 2 of 14</td>
<td>6</td>
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<tr>
<td>Gastric / Oesophageal</td>
<td><strong>EOX</strong>: Epirubicin 50mg/m², oxaliplatin 130mg/m² and d1 capecitabine 625mg/m² bd daily 21 day cycle</td>
<td>10</td>
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<tr>
<td>NHL</td>
<td><strong>CHOP or R-CHOP</strong>: Cyclophosphamide 750mg/m², doxorubicin 50mg/m², vincristine 1.4mg/m² d1 and prednisolone 100mg d1-6 of 21 day cycle</td>
<td>11</td>
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<td>R-CHOP-14 ref Cunningham et al, Lancet 2013, 381, 1817 - 1826, Rituimab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone in patients with newly diagnosed diffuse large B-cell non-Hodgkin lymphoma: a phase 3 comparison of dose intensification with 14-day versus 21-day cycle</td>
<td>5% for R-CHOP-14 with integral GCSF</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td><strong>ABVD</strong>: Doxorubicin 25mg/m², bleomycin 10,000u, vinblastine 6mg/m² and dacarbazone 375mg/m² d1 and 15 of 28 day cycle</td>
<td>2-12</td>
</tr>
<tr>
<td>Germ cell</td>
<td><strong>BEP</strong>: Bleomycin, etoposide and cisplatin (exact doses not specified from this source)</td>
<td>18</td>
</tr>
<tr>
<td>Head and neck</td>
<td><strong>TPF</strong>: Docetaxel 75mg/m², Cisplatin 75 mg/m², fluorouracil 750mg/m², d1 of 21 day cycle</td>
<td>9</td>
</tr>
</tbody>
</table>
APPENDIX 6

See suspected neutropenic sepsis admission assessment attached