**Decision Tree for Febrile Neutropenia: Medical Oncology Solid Tumour and Lymphoma Patients**

**Low Risk (Appendix 1)**

- **Ciprofloxacin 750 mg PO q 12 h + Amoxicillin-Clavulanate 500 mg PO q 8 h.** If penicillin allergy, ciprofloxacin 750 mg PO q 12 h as monotherapy. (Appendix 2)

**High Risk**

- **Cefazidime 1 g IV q 8 h +/- vancomycin (for increased gram-positive coverage) or Piperacillin/Tazobactam 4.5 g IV q 6 h or imipenem-cilastatin 500 mg IV q 6 h. Initiate vancomycin under the conditions outlined in Appendix 2**

**No defined focus**

- **Ciprofloxacin 400 mg IV q 12 h + Vancomycin 1 g IV q 12 h (this regimen not recommended if receiving prophylactic fluoroquinolone. Choose alternative gram-negative coverage)** (Appendix 2)

**No penicillin allergy**

- **Afebrile for greater than or equal to 48 hours**

  - Discontinue antibiotics if clinically well, no focus of infection and cultures negative. Monitor, reassess.

- **ANC greater than or equal to 0.5 x 10^9 cells/L for greater than or equal to 48 hours**

  - Initially low risk. Discontinue antibiotics when afebrile 5 to 7 days if no complications. Monitor, reassess.

  - Initially high risk. Continue antibiotics until ANC greater than or equal to 0.5 x 10^9 cells/L or for 2 weeks total therapy. Monitor, reassess.

**Penicillin allergy**

- **Afebrile for greater than or equal to 48 hours**

  - Discontinue antibiotics if clinically well, no focus of infection and cultures negative. Monitor, reassess.

- **ANC less than 0.5 x 10^9 cells/L for greater than or equal to 48 hours**

  - Condition stable. Continue antibiotics for 2 weeks. Monitor, reassess.

- **ANC greater than or equal to 0.5 x 10^9 cells/L for greater than or equal to 5 days**

  - Condition worsens, and new focus identified. Change antibiotics per C&S/SS while also maintaining gram-negative coverage. Monitor, reassess.

  - Condition worsens and no new focus identified. Consult Infectious Diseases Service if available or transfer to closest tertiary facility. May consider empiric antifungal if still febrile after 4 days.

**No defined focus**

- **Afebrile for greater than or equal to 48 hours**

  - Discontinue antibiotics if clinically well, no focus of infection and cultures negative. Monitor, reassess.

- **ANC greater than or equal to 0.5 x 10^9 cells/L for greater than or equal to 48 hours**

  - Initially low risk. Discontinue antibiotics when afebrile 5 to 7 days if no complications. Monitor, reassess.

  - Initially high risk. Continue antibiotics until ANC greater than or equal to 0.5 x 10^9 cells/L or for 2 weeks total therapy. Monitor, reassess.

**Defined Focus**

- **Duration specific for focus, S&S resolved. Until afebrile 5 to 7 days, ANC greater than and equal to 0.5 x 10^9 cells/L. Monitor, reassess.**

**Ceftazidime 1 g q8h IV**

- **Reassess after 72 hours, or sooner if indicated, based on C&S and clinical S&S (Appendix 3)**

**Ciprofloxacin 400 mg IV q12h + Vancomycin 1g IV q12h**

- **(this regimen not recommended if receiving prophylactic fluoroquinolone. Choose alternative gram-negative coverage)** (Appendix 2)

**ANC greater than or equal to 0.5 x 10^9 cells/L**

- **For greater than or equal to 5 days**

  - Reassess (Appendix 3)

**ANC less than 0.5 x 10^9 cells/L**

- **For greater than or equal to 48 hours**

  - Reassess (Appendix 3)

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**Disclaimer**

The London Health Sciences Centre (LHSC) and London Regional Cancer Program (LRCP) developed these guidelines for the purpose of assisting medical practitioners in the treatment of febrile neutropenic patients undergoing cancer chemotherapy. They apply only to solid tumours and lymphoma. They apply to inpatient management only.

These guidelines are general and the application must consider the variations in individual patients, types of infections being treated, antimicrobial susceptibility patterns, underlying causes of neutropenia, and expected time to recovery. It must be noted that no specific scheme, no specific drug or combination, and no specific period of treatment can be applied unequivocally to all patients with neutropenia and fever. LHSC will not assume any legal liability or responsibility for the accuracy, completeness, or usefulness of any information in this document.

Updated November 2014
Numerous instances when Vancomycin should be initiated immediately. These are:

- Hemodynamic instability or other evidence of severe sepsis
- Pneumonia documented radiographically
- Positive blood culture for gram-positive bacteria, before final identification and susceptibility testing is available
- Clinically suspected serious catheter related infection (e.g. chills or rigor with infusion through catheter and cell lines around the catheter entry/exit site)
- Skin or soft-tissue infection at any site
- Colonization with MRSA or cephalosporin-resistant Streptococcus pneumonia
- Severe mucositis, if fluoroquinolone prophylaxis has been given and Ceftazidime is employed as empirical therapy

### Appendix 3

Fever persisting more than 3 days and in whom no source or organism has been identified is suggestive of a non-bacterial infection, a bacterial infection resistant to the antibiotic(s) emergence of a second infection, inadequate serum and tissue levels of antibiotic, drug fever, cell wall-deficient bacteremia or infection at an avascular site, such as abscess or catheter.

Some patients with microbiologically defined bacterial infections may, however, require more than 5 days of therapy before defervescence occurs. Reassessment should include:

- Review of all previous culture results
- A meticulous physical examination
- Chest x-ray
- Status of all vascular catheters
- Additional blood cultures
- Specimens of specific sites of infection
- Diagnostic imaging of any organ suspected of having infection
- If possible, serum concentrations of antibiotics, especially aminoglycosides

### Appendix 4

Antibiotics requiring dose Adjustments in Patients with Renal Dysfunction

- Ceftazidime
- Vancomycin
- Ciprofloxacin
- Amoxicillin/Clavulanate
- Piperacillin/Tazobactam
- Imipenem-Cilastatin

Readily accessible resources to consult when determining dose reductions include the CPS, Micromedex and Lexicomp

### Appendix 1

Factors Favoring Low-Risk for Severe Infection in Febrile Neutropenia in Patient with Solid Tumors (non-hematological malignancies)

- Adjuvant Treatment
- Expected duration neutropenia of less than 7 days
- ANC greater than or equal to 1
- Non hematologic cancer
- No prior infection
- No obvious focus of infection
- No hypotension
- No confusion
- No diabetes or vomiting
- Grade 2 mucositis or less
- Compliant (needs to come in if diarrhea or vomiting or can’t take oral meds)
- Normal organ function (renal, hepatic, pulmonary, cardiac)
- No diabetes
- Does not live alone (friend or family member at home until neutropenia resolved)
- Access to medical care (less than 1 hour) and initial daily medical outpatient
- Follow-up especially re culture results

### Appendix 2

### Fever persisting more than 3 days and in whom no source or organism has been identified is suggestive of a non-bacterial infection, a bacterial infection resistant to the antibiotic(s) emergence of a second infection, inadequate serum and tissue levels of antibiotic, drug fever, cell wall-deficient bacteremia or infection at an avascular site, such as abscess or catheter.

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### Appendix 4

Vancomycin Use

There are some instances when Vancomycin should be initiated immediately. These are:

- Hemodynamic instability or other evidence of severe sepsis
- Pneumonia documented radiographically
- Positive blood culture for gram-positive bacteria, before final identification and susceptibility testing is available
- Clinically suspected serious catheter related infection (e.g. chills or rigor with infusion through catheter and cell lines around the catheter entry/exit site)
- Skin or soft-tissue infection at any site
- Colonization with MRSA or cephalosporin-resistant Streptococcus pneumonia
- Severe mucositis, if fluoroquinolone prophylaxis has been given and Ceftazidime is employed as empirical therapy