INITIAL INPATIENT MANAGEMENT OF NEUTROPENIC FEVER

Prepared by Antimicrobial Stewardship Program, Pharmacy, ICT consultation service, and Division of Hematology/Oncology

**Signs/Symptoms:**
- Single temp ≥101 or temp ≥100.4 on 2 consecutive measurements OR evidence of hemodynamic instability/ signs of early early sepsis
- ANC < 500 or expected to be <500 in next 48hrs
- High-risk patient* (anticipated neutropenia >7 days, clinical instability, or medical comorbidities)

*Classical signs/symptoms may be absent, especially early in the clinical course- use clinical judgment at all times; maintain a low threshold for antibiotics in patients who do not fit the above criteria but are clinically concerning

**Obtain:**
- 2 sets of blood cultures
- Urinalysis and urine culture
- CXR (PA and lateral if patient able)
- Stool for C. diff, if diarrhea present
- Flu/RSV PCR, if negative, then respiratory viral panel (RVP), if seasonally appropriate

**One of the following present*: **
- Severe sepsis or hemodynamic instability
- Pneumonia documented on imaging
- Blood culture + for gram positive organism and identification/sensitivities pending
- Suspected serious catheter related infection (i.e., chills with infusion, cellulitis at insertion site)
- Skin or soft tissue infection
- Known colonization or previous MRSA infection or history of other multidrug resistant organisms (ID consultation recommended)

*Note: severe mucositis while receiving fluoroquinolone prophylaxis is not an indication for Vancomycin if Cefepime is given as empiric therapy

**Begin Cefepime monotherapy**

<table>
<thead>
<tr>
<th>Crd (ml/min)</th>
<th>Dosage</th>
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</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>2g q8hrs</td>
</tr>
<tr>
<td>30-60</td>
<td>1g IV q8hrs or 2g IV q12hrs</td>
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<tr>
<td>10-29</td>
<td>1g IV q12hrs or 2g IV q24hrs</td>
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<tr>
<td>&lt;10</td>
<td>1g IV q24hrs</td>
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<tr>
<td>HD</td>
<td>2g IV after HD</td>
</tr>
<tr>
<td>CVVH</td>
<td>2g IV q12hrs</td>
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**Begin Cefepime AND Vancomycin**

- See Cefepime dosing under monotherapy
- Dose Vancomycin per nomogram

**Afebrile**
- Continue Cefepime monotherapy; see back for discontinuation parameters

**Still febrile after 48-72hrs of empiric therapy**
- Consider ID consult for adjustment in antimicrobial regimen and further work up

**No**

**Yes**

- Re-evaluate empiric antibiotics at 48hours
- Consider discontinuing Vancomycin if cxs negative for MRSA

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*Neutropenic patients may not mount an inflammatory response to infection so classical exam findings may be absent

- **Penicillin allergy:** cross reaction with Cephalosporins is low (2-3%)
  - If mild penicillin allergy, not IgE mediated, treat with Cefepime 2g IV with close monitoring
  - If anaphylaxis/IgE mediated allergy (hives, bronchospasm, angioedema), treat with Aztreonam 2g IV +/- Gentamicin 3-5mg/kg IV (for enhanced coverage of MDROs if severe infection/sepsis) + Vancomycin per nomogram (for GP coverage)

- **If clinical suspicion for Clostridium difficile infection:**
  - Send stool for testing
  - Place patient in “contact plus” isolation
  - Begin empiric treatment with Metronidazole PO/IV 500mg q8hrs or Vancomycin PO 125mg q6hrs (based on severity of illness)

- **If clinical suspicion for other intra-abdominal source:**
  - Consider adding anaerobic coverage with Metronidazole 500mg IV/PO q8hrs or changing Cefepime to Piperacillin/tazobactam 2.25-4.5g IV
  - Consider CT abdomen/pelvis

- **If clinical suspicion for pneumonia based on symptoms and xray findings:**
  - Send sputum culture, urine legionella antigen and urine strep pneumo antigen
  - Begin Cefepime and Vancomycin as indicated on page 1

- **If clinical suspicion for meningitis/encephalitis:**
  - Perform LP - send CSF for cell count/diff, protein, glucose, bacterial culture, HSV PCR
    - Consider other studies based on clinical picture
  - Consider adding Vancomycin per nomogram, Ampicillin 2g IV q4hrs, +/- Acyclovir 10mg/kg IBW IV
  - Obtain ID consult

- **If clinical suspicion for Influenza, RSV or other respiratory viral illness:**
  - Obtain Flu/RSV PCR, if negative consider respiratory viral panel (RVP)
  - Place patient in droplet isolation (influenza) or contact isolation (RSV – use mask, gloves, gown for close patient contact; pull curtain closed in shared rooms)
  - If Influenza positive, begin Oseltamivir (needs Stewardship approval)
  - If pt in shared room and flu positive, treat exposed roommate with prophylactic course of Oseltamivir

- **If clinical suspicion for skin/soft tissue infection:**
  - If mild/moderate, begin Cefepime and Vancomycin as indicated on page 1
  - If severe infection or concern for necrotizing fasciitis:
    - Add Clindamycin 900mg q8hrs
    - Recommend surgical consultation for debridement/drainage

- **If clinical suspicion for oral/dental infection:**
  - Begin Clindamycin 600mg IV q8hrs in addition to Cefepime

- **Duration of antibiotics***:
  - **Documented infections:**
    - Continue antibiotics for appropriate duration of underlying infection
    - Should continue at least until ANC >500 and rising or;
    - If appropriate treatment course completed and signs/symptoms resolved, patients can be changed to fluoroquinolone prophylaxis until marrow recovery
  - **No documented infection:**
    - Continue regimen until patient afebrile and ANC >500 and rising

*Clinical Practice Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Disease Society of America*