CHI Franciscan Health Febrile Neutropenia Algorithm

**Neutropenic Fever**
- Absolute Neutrophil Count (ANC) <500 cells/mm³ OR
- ANC expected to fall below 500 cells/mm³ during next 48 hours AND
- A single oral temperature ≥ 38.3 °C (101 °F) OR
- Oral temperature ≥ 38° C (100.4°F) sustained over 1 hour

If source is known, treat according to IDSA recommendations

Empiric Therapy (unknown source)

Hemodynamically Stable (admitted to med/surg)
- Cefepime 2 grams IV q8hrs

Hemodynamically Unstable (sepsis) and/or ICU/PCU
- Meropenem 1 gram IV q8hrs
- Levofloxacin 750mg IV daily OR Aminoglycoside per Pharmacy
- Vancomycin per Pharmacy

Acute Lymphoid Leukemia or post stem cell transplant or high-dose steroids (≥20mg/day Prednisone) or high risk neutropenia expected to last >7 days
- Meropenem 1 gram IV q8hrs
- Levofloxacin 750mg IV daily OR Aminoglycoside per Pharmacy
- Vancomycin per Pharmacy

MDR Risk
- Suspected intra-abdominal source
- Hx of resistant gram negative bacteria or ESBL + organism
- Exposure to a family member with MDR pathogen
- Received >48hrs of broad spectrum antibiotics in last 90 days (e.g. Pip/Tazo, Cefepime, Meropenem, etc.)

**If indicated:**
- Metronidazole (for GI and perirectal symptoms)
- Acyclovir for mucosal lesions/ulceration
- ± Vancomycin*
- ± Antifungal therapy**

Approved by ASP committee
Last Updated July 2014
**MRSA Coverage**

<table>
<thead>
<tr>
<th>Consider if:</th>
<th>Recommended</th>
<th>Alternative</th>
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<tbody>
<tr>
<td>• Suspected catheter-related infection</td>
<td>Vancomycin (goal trough 15-20)</td>
<td>Daptomycin</td>
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<td>• Skin or soft tissue</td>
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<td>Linezolid</td>
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<tr>
<td>• Pneumonia</td>
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<td>(can cause marrow suppression &amp; is bacteriostatic)</td>
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<td>• Hemodynamic instability (sepsis)</td>
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<td>• Bacterial colonization and/or resistance (MRSA or pen-resistant S.pneumo)</td>
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Although isolation of gram-positive organisms is more common, gram-negative organisms are associated with greater mortality (5% vs 18%)

**Antifungal Coverage:** Fungi rarely cause fever early in the course of neutropenia; rather, they are encountered after the first week of prolonged neutropenia and empirical antibiotic therapy

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<tr>
<td>• Mouth/mucosal (e.g. thrush) or esophageal (e.g. retrosternal burning) symptoms at initial presentation</td>
<td>If candida suspected (recurrent fevers after 4 days of abx therapy): Fluconazole</td>
<td>Micafungin</td>
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<tr>
<td>• Hemodynamically unstable after initial doses of empiric antibacterial therapy</td>
<td>If aspergillus*** suspected (recurrent fevers after 7 days of abx therapy): Voriconazole</td>
<td>Amphterican B</td>
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<tr>
<td>• Recurrent fever after 4-7 days of empiric therapy</td>
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<td>❖ Micafungin should replace Fluconazole for treatment or history of C. glabrata and/or recent fluconazole prophylaxis</td>
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<td>• Cultures or imaging suggest potential fungal infection</td>
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<td>• Positive serum fungal markers (glucan or galactomannan)</td>
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***Aspergillus can cause life-threatening infection of the sinuses and lungs after ≥ 2 weeks of neutropenia

Antibiotic Escalation/De-escalation (3-5 days after empiric therapy started):

1. **Responding/clinically stable:** decreasing fever trend, S/S of infection are stable or improving, hemodynamically stable
   a. No change to antibiotic regimen
   b. Stop MRSA coverage if cultures do not show MRSA

2. **Not responding/clinically unstable**
   a. Broaden antimicrobial coverage to further cover resistant GNR (e.g. change Cefepime to Meropenem).
   b. Ensure coverage includes anaerobes
   c. Add anti-fungal coverage
   d. Consider ID consult
   e. **Unexplained persistent fever in a patient who is otherwise stable** does not require a change to empiric regimen, escalation of therapy is rarely indicated.

**Duration**

- Therapy duration should be based on specific organism and site of infection (see durations of therapy recommendations in IDSA guidelines)
- **Pt afebrile for ≥72hrs:** If ANC > 500 may DC abx if no infection identified. If ANC < 500 continue abx at least for 7 days or ideally until ANC > 500 (may consider changing to PO treatment with Levofoxacin+ Amp/Clav if patient is low risk).
- **In patients with persistent fever ( unidentified source or organism):** continue initial regimen until bone marrow recovery indicated by ANC > 500 cells/mm³