Febrile Neutropenia Algorithm for High Risk Adult Patients – No Allergy
(AML, ALL, AlloSCT, expected ANC < 500 for ≥ 10 days, GVHD with steroids > 20 mg/day, alemtuzumab therapy)

**Septic Shock?** Hemodynamic instability/new organ dysfunction*

- **Pip/tazo or Cefepime + Amikacin (A) + Vancomycin (V)**
  - Pip/tazo preferred if concern for intra-abdominal or peri-rectal source, oropharyngeal abscess, or VRE colonized.

- **Recommend discontinuing A and V after 48 hours if hemodynamically stable, vancomycin criteria not met, and cultures are negative for a bacteria requiring A or V**

- **If still febrile at 96 hours, assess antifungal prophylaxis**

- **At day 5 if afebrile for ≥ 48 hours and hemodynamically stable, assess appropriateness of antimicrobials using de-escalation guide on page 2**

**Vancomycin Criteria:**
Cellulitis
Pneumonia documented radiographically
- Obtain sputum culture or MRSA nasal swab culture (to determine colonization status) – if negative for MRSA, may discontinue vancomycin
- Recommend 7 days vancomycin duration for pneumonia
Catheter-related infection
- Chills/fever with flushing catheter, catheter site infection, positive blood culture
MRSA colonization or prior infection

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**Signs and Symptoms of Sepsis**
- SBP < 90 mmHg or MAP < 65 mmHg
- Creatinine increase > 0.5 mg/dL
- Acute oliguria
- Hyperlactatemia
- Altered mental status

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**If fluconazole**

- Initiate antifungal treatment of febrile neutropenia by changing fluconazole to micafungin.

- If breakthrough fevers and/or respiratory symptoms are present, obtain chest CT. If consistent invasive mold infection and/or galactomannan (GM) positive, change fluconazole to voriconazole.

- If still febrile 96 hours after switch, evaluate:
  - Respiratory symptoms
  - Pattern of breakthrough fever
  - GM (if not already done)

- Continue current therapy and monitor if:
  - Single episode of breakthrough fever
  - No respiratory symptoms
  - Negative GM
  - Clinically stable

- If multiple episodes of breakthrough fever, no respiratory symptoms, and negative GM, change antibacterial agent to meropenem.

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**If posaconazole**

- Evaluate the following:
  - Posaconazole trough concentration
  - Chest imaging
  - History of azole exposure
  - Pattern of breakthrough fever
  - Evidence of candida infection (e.g. thrush, vaginal candidiasis, dermatitis)

- If chest CT consistent with invasive mold infection and posaconazole trough is adequate for prophylaxis, consider ID consult and change posaconazole to Ambisome.

- Considering continuing posaconazole and monitoring if:
  - Chest CT is negative
  - Posaconazole trough is adequate for prophylaxis
  - Single episode of breakthrough fever
  - Clinically stable

- If still febrile 96 hours after switch, assess antifungal prophylaxis

- Consider adding metronidazole to cefepime or changing antibacterial to meropenem if:
  - Limited azole exposure (< 14 days, counting prior admissions)
  - Multiple episodes of breakthrough fever
  - Suspicion for typhlitis or neutropenic enterocolitis
On **day 5** of therapy, assess appropriateness of antimicrobials and **consider de-escalation in the following patients:**

- Hemodynamically and clinically stable
- Afebrile for ≥48 hours
- Appropriate infectious diagnostic work-up (e.g., 2 sets of blood cultures [central and peripheral], urine/respiratory/wound cultures as appropriate, imaging as appropriate)
- Regardless of ANC recovery

**Low Suspicion for Bacterial Infection:**
- Negative bacterial cultures
- No evidence of bacterial infection on imaging or physical exam

**Suspected Bacterial Infection:**
- Negative bacterial cultures
- Laboratory, imaging or physical findings indicative of possible infection

**Documented Bacterial Infection:**
- Positive cultures and imaging or physical exam consistent with infection

**Treatment Recommendation:**
- Discontinue antibiotic therapy

**Treatment Recommendation:**
- Tailor antibiotic therapy to suspected source of infection
- Once an appropriate duration is completed for suspected source of infection, discontinue antibiotic therapy

**Treatment Recommendation:**
- Tailor antibiotic therapy to documented source of infection based on culture and sensitivity results (e.g., if gram positive or fungal organism is isolated, discontinue antipseudomonal gram negative therapy and tailor therapy based on susceptibilities)
- Once an appropriate duration is completed for documented infection, discontinue antibiotic therapy

Resume afebrile neutropenia prophylaxis if indicated

- Monitor patient for signs and symptoms of infection after discontinuation/de-escalation of antibiotic therapy
- Reinitiate febrile neutropenia algorithm if patient has a recurrent fever (≥101 °F or ≥100.4 °F over 1 hour) or meets new criteria for suspected or documented bacterial infection (page 1)

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*Antimicrobials may be discontinued prior to Day 5 evaluation at the discretion of the primary team if the fever is felt to be non-infectious (e.g., active malignancy, tumor fevers, blood transfusion, cytokine release syndrome, drug infusion reactions, differentiation syndrome, graft-versus-host disease)*