Febrile Neutropenia Algorithm for High Risk Adult Patients – MAJOR PENICILLIN ALLERGY
(AML, ALL, AlloSCT, expected ANC < 500 for > 10 days, GVHD with steroids > 20 mg/day, alemtuzumab therapy)

Major allergy includes anaphylaxis, angioedema, immediate hives: CONFIRM ALLERGY in WAKEONE is ACCURATE (discuss with patient or family)

Review of health records is warranted. If patient has tolerated cephalosporins in past, choose cefepime and refer to ‘no allergy’ algorithm.

**Septic Shock? Hemodynamic instability/new organ dysfunction**
- Meropenem + Amikacin (A) + Vancomycin (V)
- Discuss antibiotic choice with CAUSE delegate if patient also reports major allergy to cephalosporin

**Meropenem (add vancomycin only if specific criteria are met)**

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

**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.**

**Consider ID Consult if multiple episodes of breakthrough fever and work-up is negative:**
- Chest/sinus CT is negative
- GM is negative
- Posaconazole trough is adequate for prophylaxis (if applicable)

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

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

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**Yes**

**No**

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**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)

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

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**Consider changing posaconazole to micafungin if:**
- Extensive history (> 14 days) of azole exposure (posaconazole or fluconazole)
- Multiple episodes of breakthrough fever
- Evidence of candida infection

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**Initiate antifungal treatment of febrile neutropenia by changing fluconazole to voriconazole.**

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**If fluconazole**

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

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Discuss antibiotic choice with CAUSE delegate if patient also reports major allergy to cephalosporin.
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).

Febrile Neutropenia De-escalation Guide

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)

$^5$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)