Neutropenic Fever\(^1\) Inpatient Adult Treatment (Hematologic Cancers including Lymphoma/Myeloma)

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Note: This algorithm should not be used for patients receiving chimeric antigen receptor (CAR) cell therapy.

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Patient presents with fever or develops fever at MD Anderson

- Does patient exhibit \(\geq 2\) qSOFA criteria?\(^2\)
  - Yes → See Adult Sepsis Management algorithm and use sepsis order set
  - No → Does patient have pneumonia?
    - Yes → See Pneumonia in Adult Patients with Cancer algorithm
    - No → See Pages 2-4 for antibiotic regimen

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CVAD = central venous access device

\(^1\)ANC < 1 K/microliter and temperature either \(\geq 38.3^\circ\)C or equal to \(38^\circ\)C for 1 hour or longer

\(^2\)qSOFA criteria:
- Altered mental status
- Respiratory rate \(\geq 22\) bpm
- Systolic blood pressure \(\leq 100\) mmHg
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**FINDINGS**

- Neutropenic fever
- Suspected line infection
- MRSA colonization/ skin and soft tissue infection/mucositis greater than or equal to grade 2

**ANTIMICROBIAL THERAPY RECOMMENDATIONS**

(Adjust dose for patients with renal/hepatic dysfunction)

**Gram negative coverage antibiotics should be given first**

Antibiotics should be given within 2 hours

- **Choose one:**
  - Cefepime 2 grams IV every 8 hours or
  - Piperacillin and tazobactam 4.5 grams IV every 6 hours or
  - Meropenem 1 gram IV every 8 hours

If indicated for double gram negative coverage, add either:

- Amikacin 15 mg/kg IV once and then repeat per pharmacokinetic data or
- Ciprofloxacin 400 mg IV every 8 hours only if no quinolone prophylaxis

**Documented beta-lactam allergy (i.e., hives or anaphylaxis):** see Page 4

- **Choose one:**
  - Cefepime 2 grams IV every 8 hours or
  - Piperacillin and tazobactam 4.5 grams IV every 6 hours or
  - Meropenem 1 gram IV every 8 hours

**Plus:**

- Vancomycin 15 mg/kg (round to nearest 250 mg dose) IV every 12 hours or
- Daptomycin 6 mg/kg IV every 24 hours (if no evidence of pneumonia)

If indicated for double gram negative coverage, add either:

- Amikacin 15 mg/kg IV once and then repeat per pharmacokinetic data or
- Ciprofloxacin 400 mg IV every 8 hours only if no quinolone prophylaxis

**Documented beta-lactam allergy (i.e., hives or anaphylaxis):** see Page 4

- **Choose one:**
  - Piperacillin and tazobactam 4.5 grams IV every 6 hours or
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  - Meropenem 1 gram IV every 8 hours

**Plus:**

- Vancomycin 15 mg/kg (round to nearest 250 mg dose) IV every 12 hours or
- Daptomycin 6 mg/kg IV every 24 hours (if no evidence of pneumonia) or
- Linezolid 600 mg IV every 12 hours

If indicated for double gram negative coverage, add either:

- Amikacin 15 mg/kg IV once and then repeat per pharmacokinetic data or
- Ciprofloxacin 400 mg IV every 8 hours only if no quinolone prophylaxis

**Documented beta-lactam allergy (i.e., hives or anaphylaxis):** see Page 4

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1. MDROs include:
   - Enterococcus resistant to vancomycin
   - Staphylococcus aureus resistant to methicillin (oxacillin)
   - S. pneumoniae resistant to penicillin and streptococci resistant to ceftriaxone
   - Stenotrophomonas maltophilia
   - Any extended spectrum beta-lactamase (ESBL)-producing gram negative bacilli
   - Any carbapenem resistant gram negative bacilli
   - All other gram negative bacilli that are resistant to usual recommended first-line agents
2. Chills, rigor with infusion through catheter, cellulitis or discharge around the line entry site
3. Continue G-CSF if patient was receiving as daily prophylaxis. Consider therapeutic use if risk factor(s) present: sepsis, age > 65 years old, pneumonia or other documented infection, invasive fungal infection, ANC < 100 K/microliter, expected neutropenia duration > 10 days, uncontrolled primary disease, hospitalization at the time of fever or prior episode of NF.
4. Consider adding meropenem/diazok 500 mg IV every 8 hours to cefepime for possible intra-abdominal infection or if anaerobic coverage is necessary.
5. Consider meropenem if patient has any of the following:
   - Non-IGE-mediated allergy to alternative agents
   - Recent treatment (>= 3 days duration) with cefepime or piperacillin/tazobactam within past 30 days
   - Infection with ESBL organism
6. Infection with organism only susceptible to carbapenem
7. Double gram negative coverage should be considered with complicated tissue-based infections, neutropenic enterocolitis, and perirectal infections
8. Not preferred for blood stream infections

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Department of Clinical Effectiveness V2
Approved by the Executive Committee of the Medical Staff on 05/28/2019
**FINDINGS**

- **VRE colonization or infected patients**
  - **Stenotrophomonas maltophilia**
    - Consider adding one of the following antibiotics to one of the regimens listed on Page 2 or 4:
      - Sulfamethoxazole and trimethoprim (TMP) 5 mg/kg TMP IV or PO every 8 hours or
      - If sulfa allergy, minocycline 200 mg IV once, then 100 mg IV or PO every 12 hours
    - Consider Infectious Diseases consult

- **MDRO**
  - Consider Infectious Diseases consult

- **Consider using one of the following antibiotics, in place of vancomycin (if prior known sensitivities), with one of the regimens listed on Page 2 or 4:**
  - Daptomycin 10 mg/kg IV every 24 hours (if no evidence of pneumonia) or
  - Linezolid 600 mg IV every 12 hours

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**ANTIMICROBIAL THERAPY RECOMMENDATIONS**

(Adjust dose for patients with renal/hepatic dysfunction)

- Gram negative coverage antibiotics should be given first

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**MDRO**

- Enterococcus resistant to vancomycin
- Staphylococcus aureus resistant to methicillin (oxacillin)
- *S. pneumoniae* resistant to penicillin and streptococci resistant to ceftriaxone
- Stenotrophomonas maltophilia
- Any extended spectrum beta-lactamase (ESBL)-producing gram negative bacilli
- Any carbapenem resistant gram negative bacilli
- All other gram negative bacilli that are resistant to usual recommended first-line agents

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2**Not preferred for blood stream infections**
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### (Hematologic Cancers including Lymphoma/Myeloma)

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### FINDINGS

- **Serious documented beta-lactam allergy** (i.e., hives or anaphylaxis)
- **Neutropenic fever**
- **Suspected line infection**¹ and/or bacteremia
- **MRSA colonization/skin and soft tissue infection**
- **Mucositis greater than or equal to grade 2**

### ANTIMICROBIAL THERAPY RECOMMENDATIONS

*(Adjust dose for patients with renal/hepatic dysfunction)*

#### Gram negative coverage antibiotics should be given first

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**Note:**

1. Double gram negative coverage recommended due to reduced gram negative pathogen susceptibility to aztreonam according to local antibiograms
2. Not preferred for blood stream infections
3. Chills, rigors with infusion through catheter, or cellulitis or discharge around the line entry site

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See Page 5 for re-assessment.
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RE-ASSESSMENT

Patient afebrile

72-hour evaluation

Patient febrile

Has source of fever been identified?

Yes

Treat for appropriate duration based on nature of infection (e.g., urinary tract infection, cellulitis)

No

Continue treatment for 2 days after ANC > 0.5 K/microliter and rising

● Check susceptibilities
● Make necessary changes in antibiotic regimen
● CT scans, serology and other diagnostic work-up as clinically indicated
● Consider or re-evaluate antifungals and/or antivirals

Yes

Has source of fever been identified?

Yes

Repeat cultures
● CT sinuses and chest, CMV PCR and aspergillus antigen, other diagnostic work-up as clinically indicated
● Re-evaluate antibiotics
● Consider antifungals and/or antivirals

No

No

Does fever persists?

Yes

Consider Infectious Diseases consult, CT chest and/or other diagnostic tests if clinically indicated

Disposition based on Infectious Diseases consult recommendations and/or diagnostic test results

No

Observe; monitor ANC as well as culture and sensitivity results; chest x-ray remains negative

Complete antibiotic regimen and disposition per MD

Reassess at Day 5

1 Consider narrowing therapy based on cultures and sensitivities (e.g., discontinue anti-MRSA or anti-VRE agents if no gram positive organisms are identified and patient does not have cellulitis)

2 Consider transition to antimicrobial prophylaxis if otherwise indicated and no clear infectious source of fever was identified
SUGGESTED READINGS


Continued on next page
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SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


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(Hematologic Cancers including Lymphoma/Myeloma)

This practice consensus algorithm is based on majority expert opinion of the Neutropenic Fever Work Group at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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Ella Ariza Heredia, MD (Infectious Disease)
Samuel L. Aitken, PharmD (Pharmacy Clinical Programs)
Alison Gulbis, PharmD (Pharmacy Clinical Programs)
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Terry W. Rice, MD (Emergency Medicine)
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