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

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. Local microbiology and susceptibility/resistance patterns should be taken into consideration when selecting antibiotics. This algorithm should not be used to treat pregnant women.

Note: This algorithm should also be used for patients receiving chimeric antigen receptor (CAR) T-cell therapy.

### PRESENTATION

Patient with neutropenia and fever

### ASSESSMENT

- Physical exam
- IV hydration
- CBC with differential, basic metabolic panel, lactic acid
- Blood cultures (with a set collected from each lumen simultaneously if CVAD present and 1 peripheral site)
- Other cultures (e.g., sputum culture, respiratory viral PCR panel, urinalysis/urine culture), only if clinically indicated
- MRSA nasal swab (if pneumonia suspected or confirmed)
- Chest x-ray
- Other tests as clinically indicated

See Inpatient Sepsis Management - Adult algorithm and use sepsis ordering tools

### FINDINGS

Does patient have pneumonia?

- Yes
- See Pneumonia in Adult Patients with Cancer algorithm

- No
- See Pages 2-3 for antibacterial recommendations

---

\(^1\) Criteria:
- Absolute neutrophil count (ANC) ≤ 0.5 K/microliter and temperature either ≥ 38.3°C or equal to 38°C for 1 hour or longer or
- ANC ≤ 1 K/microliter and an expected decline to ≤ 0.5 K/microliter over 48 hours and temperature either ≥ 38.3°C or equal to 38°C for 1 hour or longer

See Inpatient Sepsis Management - Adult algorithm for sepsis screening criteria

---

CVAD = central venous access device
PCR = polymerase chain reaction
MRSA = methicillin-resistant *Staphylococcus aureus*

---

Copyright 2022 The University of Texas MD Anderson Cancer Center

Department of Clinical Effectiveness V3
Approved by the Executive Committee of the Medical Staff on 03/09/2022
Consider expanded gram positive coverage if mucositis

For selecting antibacterial therapy consider the following:

- Recent culture and sensitivity results
- History of resistant gram negative organism\(^2\) infection or colonization
- Suspected line infection\(^3\)
- Recent antibiotic history and prophylaxis
- Source of infection, if identified
- Organ dysfunction
- Mucositis \(\geq 2\)

Consider the use of therapeutic G-CSF if risk factors are present (see Appendix A).

\(^{1}\) For serious documented beta-lactam allergy, see Page 3

\(^{2}\) Refer to \(\text{institutional renal dosing guide}\) (internal only) or tertiary dosing references (\(e.g.,\) Lexicomp) for dosing recommendations

\(^{3}\) Resistant gram negative organisms include:

- \textit{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

\(^{4}\) Chills, rigors with infusion through catheter, cellulitis or discharge around the catheter entry site

\(^{5}\) Consider expanded gram positive coverage if mucositis \(\geq 2\) and on fluoroquinolone prophylaxis and on cefazidime as empiric therapy. Isolated mucositis is not an indication for expanded gram positive coverage.

VRE = vancomycin-resistant enterococcus

**Antibacterial Recommendations**

**Antibacterial Recommendations**

(Adjust dose for patients with renal/hepatic dysfunction)

Gram negative coverage antibiotics should be given first. Antibiotics should be given within 1 hour.

- If suspected line infection\(^3\) and/or bacteremia **add**:
  - Vancomycin or
  - Daptomycin (if no evidence of pneumonia)

- If MRSA colonization or skin and soft tissue infection or pneumonia or mucositis\(^5\) \(\geq 2\) **add**:
  - Vancomycin or
  - Linezolid (not preferred for MRSA blood stream infection) or
  - Daptomycin (if no evidence of pneumonia)

- If VRE colonization or infection **add**:
  - Linezolid or
  - Daptomycin (if no evidence of pneumonia)

\(\text{G-CSF} = \text{granulocyte colony stimulating factor}\)

\(\text{VRE} = \text{vancomycin-resistant enterococcus}\)
Neutropenic Fever Inpatient Adult Treatment
(Hematologic Cancers including Lymphoma/Myeloma)

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. Local microbiology and susceptibility/resistance patterns should be taken into consideration when selecting antibiotics. This algorithm should not be used to treat pregnant women.

SERIOUS DOCUMENTED BETA-LACTAM ALLERGY
(anaphylaxis, hives, or serious non-IgE mediated drug reactions¹)

ASSESSMENT

- For selecting antibacterial therapy consider the following
  - Recent culture and sensitivity results
  - History of resistant gram negative organism² infection or colonization
  - Suspected line infection⁴
  - Recent antibiotic history and prophylaxis
  - Source of infection, if identified
  - Organ dysfunction
  - Mucositis ≥ grade 2
  - Consider the use of therapeutic G-CSF if risk factors are present (see Appendix A)

ANTIBACTERIAL RECOMMENDATIONS²
(Adjust dose for patients with renal/hepatic dysfunction)

For gram negative coverage antibiotics should be given first. Antibiotics should be given within 1 hour.

For gram negative coverage select:
- Aztreonam³
  - Plus:
    - Amikacin or
    - Ciprofloxacin (only if no quinolone prophylaxis)

For anaerobic coverage in the setting of neutropenic enterocolitis, perirectal infections or mucositis ≥ grade 2 add:
- Metronidazole

For gram positive coverage select from the following findings

If suspected line infection⁴ and/or bacteremia select one of the following:
- Vancomycin or
- Daptomycin (if no evidence of pneumonia)

If MRSA colonization or skin and soft tissue infection select one of the following:
- Vancomycin or
- Linezolid (not preferred for MRSA blood stream infections) or
- Daptomycin (if no evidence of pneumonia)

If none of the above, select one of the following:
- Vancomycin or
- Linezolid

See Page 4 for re-assessment

1 Examples of non-IgE mediated drug reactions include Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS)

2 Refer to institutional renal dosing guide (internal only) or tertiary dosing references (e.g., Lexicomp) for dosing recommendations

3 Resistant gram negative organisms include:
  - 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

4 Chills, rigors with infusion through catheter, cellulitis or discharge around the catheter entry site

5 Double gram negative coverage recommended due to reduced gram negative pathogen susceptibility to aztreonam according to local antibiograms

Copyright 2022 The University of Texas MD Anderson Cancer Center

Approved by the Executive Committee of the Medical Staff on 03/09/2022
Neutropenic Fever Inpatient Adult Treatment
(Hematologic Cancers including Lymphoma/Myeloma)

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. Local microbiology and susceptibility/resistance patterns should be taken into consideration when selecting antibiotics. This algorithm should not be used to treat pregnant women.

RE-ASSESSMENT

Patient afebrile

Has source of fever been identified?

Yes

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

If all of the following criteria are met for 48-72 consecutive hours, consider short (≤ 5 days) course of antimicrobial therapy and resume antimicrobial prophylaxis if neutropenia not resolved

- Resolution of signs and symptoms of infection and
- Normal vital signs and
- Apyrexia

No

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

Has source of fever been identified?

Yes

Re-evaluate at 72-96 hours from onset of neutropenic fever

No

Repeat cultures
- CT chest, aspergillus antigen, and/or other diagnostic work-up as clinically indicated
- Re-evaluate antibiotics
- Consider antifungal and/or antivirals
- Consult Infectious Diseases

Patient febrile

Has source of fever been identified?

Yes

No

Consider transition to antimicrobial prophylaxis if otherwise indicated and no clear infectious source of fever is identified

TREATMENT

1 Refer to institutional renal dosing guide (internal only) or tertiary dosing references (e.g., Lexicomp) for dosing recommendations

2 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)

3 In the absence of steroids or antipyretics

4 Consider transition to antimicrobial prophylaxis if otherwise indicated and no clear infectious source of fever is identified

Reassess at Day 5

- If afebrile, disposition per Primary Team and reassess as clinically indicated
- If febrile, consult Infectious Diseases if not already consulted for further work-up and disposition
APPENDIX A: Potential Indications for use of Therapeutic G-CSF

Consider therapeutic use if the following risk factor(s) are present:

- Sepsis
- Age > 65 years old
- Pneumonia or other documented infection
- Invasive fungal infection
- ANC < 100 K/microliter
- Expected neutropenia duration > 10 days
- Hospitalization at the time of fever or prior episode of neutropenic fever

Note: Continue G-CSF if patient was receiving as daily prophylaxis.
SUGGESTED READINGS


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

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

Antimicrobial Stewardship Team
Javier Adachi, MD (Infectious Diseases)
Wendy Garcia, BS
Alison Gulbis, PharmD (Pharmacy Clinical Programs)
Alexandra Hacker, MSN, APRN, FNP-BC
Ella Ariza Heredia, MD (Infectious Diseases)
Tami N. Johnson, PharmD (Pharmacy Clinical Programs)
Kayleigh Marx, PharmD (Pharmacy Clinical Programs)
Joseph L. Nates, MD (Critical Care & Respiratory Care)
Adrienne Sevin, PharmD (Pharmacy Clinical Programs)

T Core Development Lead
* Clinical Effectiveness Development Team

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. Local microbiology and susceptibility/resistance patterns should be taken into consideration when selecting antibiotics. This algorithm should not be used to treat pregnant women.

DEVELOPMENT CREDITS