Neutropenic Fever\(^1\) Inpatient Adult Treatment (Solid Tumors)

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: For patients receiving chimeric antigen receptor (CAR) T-cell therapy, please refer to the Neutropenic Fever Inpatient Adult Treatment (Hematologic Cancers including Lymphoma/Myeloma) algorithm for management.

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**PRESENTATION**

Patient with neutropenia **and** fever

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**ASSESSMENT**

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

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**FINDINGS**

See Neutropenic Fever Outpatient Treatment for Solid Tumor Patients algorithm

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CVAD = central venous access device
MRSA = methicillin-resistant *Staphylococcus aureus*

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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

2. See Inpatient Sepsis Management – Adult algorithm for sepsis screening criteria

3. Patient must have a MASCC Risk Index Score of ≥ 21 and no other complicating risk factors and meet the following criteria listed below for outpatient treatment:
   - Solid tumor
   - Able to tolerate oral medications
   - Able to tolerate fluids
   - Does not use feeding tube as primary route for nutrition and medications
   - No confirmed focus of infection
   - Resides within 1 hour travel time of MD Anderson
   - Has a 24-hour caregiver
   - Has access to transportation and telephone at residence
   - Not currently on antibiotics
   - Age ≥ 18 years
   - No quinolone allergy for oral regimens
   - No history of non-compliance
   - No fluoroquinolone-resistant or multi-resistant organism colonization

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Department of Clinical Effectiveness V3

Approved by the Executive Committee of the Medical Staff on 03/09/2022
# Neutropenic Fever Inpatient Adult Treatment

## (Solid Tumors)

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## ASSESSMENT

- **Consider the following when selecting antibiotics:**
  - Recent culture and sensitivity results
  - History of resistant gram negative organisms or colonization
  - Suspected line infection
  - Recent antibiotic history and prophylaxis
  - Source of infection, if identified
  - Antibiotic allergies
  - Organ dysfunction
  - Mucositis ≥ grade 2
  - Consider the use of therapeutic granulocyte colony stimulating factor (G-CSF) if risk factors are present (see Appendix A).

## ANTIBACTERIAL RECOMMENDATIONS

### (Adjust doses for patients with renal/hepatic dysfunction)

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

Antibiotics should be given within 1 hour.

### Neutropenic fever:

- Aztreonam (preferred) or
- Ciprofloxacin if no fluoroquinolone prophylaxis or therapy in past 90 days

#### Plus:

- Vancomycin

### If mucositis ≥ grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:

- Add metronidazole

### If history of resistant gram negative organism infection:

- Consider Infectious Diseases consult

### Neutropenic fever:

- Cefepime

#### If mucositis ≥ grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:

- Add metronidazole

#### If clinically suspected line infection, bacteremia, skin/soft tissue infection or pneumonia, and/or MRSA colonization:

- Add vancomycin

#### If history of resistant gram negative organism infection:

- Consider Infectious Diseases consult
- Consider meropenem if clinically appropriate in place of cefepime/metronidazole

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

2 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

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

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

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
   - Infection with organism only susceptible to carbapenem
Re-evaluate at 72-96 hours from onset of neutropenic fever

Has source of fever been identified?

Yes

Patient febrile

TREATMENT

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

No

Patient afebrile

- Check susceptibilities
- Make necessary changes to antimicrobial therapy
- 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 antifungals
- Repeat cultures
- CT chest and other imaging as clinically indicated
- Evaluate thoroughly for non-infectious causes of fever (e.g., medications, thrombosis, tumor, necrosis)
- Consult Infectious Diseases

No

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

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

Reassess at Day 5 if not already consulted for further work up and disposition

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 vancomycin 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
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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.
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SUGGESTED READINGS


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:

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