# Febrile Neutropenia Inpatient Management Guidelines

*Updated 1/2026*

**1) Identify**

-Single temp ≥101 or temp ≥ 100.4 on 2 consecutive measurements OR evidence of hemodynamic instability/ signs of early sepsis (HR>100, BP <90/60, new hypoxia or significant change in hemodynamics), AND
-ANC < 500 OR expected to be <500 in next 48hrs
*Classical signs/symptoms may be absent, especially early in the clinical course- use clinical judgment at all times; maintain a low threshold to start antibiotics in patients who do not fit the above criteria but are clinically*

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**2) Obtain diagnostic workup**

-2 sets of blood cultures (8-10cc blood/culture bottle)
- Urinalysis and urine culture (if symptomatic)
- CXR (PA and lateral preferable, AP only if unable to leave the unit)
- Stool for C. diff and GI PCR, if diarrhea present
-MRSA nares PCR
-SARS-CoV2 PCR / Flu/RSV PCR, if negative, then respiratory pathogen panel (RPP)

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**3) Further assessment**

- Hemodynamically unstable?
- Gram negative bacteremia *(susceptibilities pending)*?
- >7 days cefepime exposure this admission?
- Known history of infection or colonization with ESBL organism?
- ICU stay during current admission?

Yes → **Begin meropenem (see below for renal dosing)**

No → **Begin cefepime (see below for renal dosing)**

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**4) Add IV vancomycin per nomogram if one or more of the following:**

- Severe sepsis or hemodynamic instability
- Pneumonia documented on imaging
- Blood culture + for gram positive organism and identification/sensitivities pending (see below)
- Suspected serious catheter related infection (i.e., chills with infusion, cellulitis at insertion site)
- Skin or soft tissue infection
- Known colonization or previous MRSA infection or history of other multidrug resistant organisms (ID consultation recommended)

***Severe mucositis while receiving fluoroquinolone prophylaxis is not an indication for vancomycin if cefepime or meropenem are given as empiric therapy*
***If MRSA nasal PCR is negative and no other microbiologic evidence of MRSA, can discontinue empiric vancomycin*
*If blood cultures are positive for Gram positive organisms, particularly in pairs and chains, strongly consider daptomycin (+/- ampicillin) for empiric coverage of VRE. Contact ID for approval***

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**5) Re-evaluate for de-escalation or additional workup after 48-72hours of empiric therapy (assuming negative work up above)**

**Afebrile + ANC <500** → Consider the following:
- Discontinue antibiotics after 3 days of apyrexia assuming negative work up
OR
- Change to levofloxacin 500mg q24h prophylaxis until ANC >500

**Still febrile after 48-72hrs of empiric therapy** → Consider ID consult for adjustment in antimicrobial regimen and further work up (see next page)

**Afebrile + ANC >500** → Discontinue antibiotics unless documented infection on work up

# Febrile Neutropenia INPATIENT Management Guidelines

*Updated 1/2026*

## 1. Identify patients with neutropenic fever and consider their underlying risk level:

Neutropenic fever: a single temperature >101 or temp >100.4 on 2 consecutive measurements *or signs of early sepsis/hemodynamic instability* * *and* ANC <500 (or expected to be <500 in next 48hrs).

* *Classical signs/symptoms may be absent, especially early in the clinical course- use clinical judgment at all times; maintain a low threshold for antibiotics in patients who do not fit the above criteria but are clinically concerning*

A 'High Risk' patient is defined as someone with an anticipated neutropenia >7 days, clinical instability, or multiple medical comorbidities.

## 2. Begin diagnostic workup by obtaining the following:

- Blood cultures (2 sets with 8-10cc of blood/culture bottle), urinalysis/urine culture (if symptomatic), and 2-view chest X-ray.
- If symptomatic and seasonally appropriate, obtain Flu/RSV/SARS-CoV-2 PCR or RVP.
- If diarrhea present, send stool for C. difficile and GI pathogen panel if appropriate
- If no prior h/o MRSA infection, send MRSA nasal swab

## 3. Treatment:

**a. If initial episode of febrile neutropenia this admission, begin cefepime 2g IV q8h (if CrCl>60) for empiric coverage**

Renally adjust as below:

CrCl 30-60 → 2g IV q12h
CrCl 10-29→ 1g IV q12h or 2g IV q24h
CrCl <10 or HD → 1g IV q24h
CVVH → 2g IV q12h

**b. If patient is hemodynamically unstable, has a history of ESBL infection/colonization, blood cultures positive for Gram negative bacteria (while susceptibilities pending), prior ICU stay during current admission, or patient has received >7 days of cefepime this admission, begin meropenem 500mg q6hrs (for CrCl>50) and consult ID**

Renally adjust as below:
CrCl 30-49 → 500mg IV q8h
CrCl 10-29→ 500mg IV q12h
CrCl <10 or HD → 500mg IV q24h
CVVH → 1g IV q12h

**Is the patient allergic to beta lactams?**

i. For those with any reported allergy to penicillin, begin cefepime or meropenem and monitor closely. Cross reactivity of penicillin with cephalosporins or carbapenems is exceedingly rare
ii. For those with moderate to severe allergies to cephalosporins, treat with aztreonam 2g IV q8h + IV vancomycin +/- IV amikacin 7.5mg/kg q12h (if c/f MDRO or severe sepsis)

## 4. Determine need for vancomycin coverage (in addition to cefepime or meropenem):

| **Reasons to add IV vancomycin coverage empirically in neutropenic fever** |
|---|
| Evidence of pneumonia on imaging |

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| Skin or soft tissue infection *(also consider adding clindamycin+ surgery consult if nec fasc concern)* |
| Suspected central line infection |
| Known recent prior MRSA infection |
| Gram positive bacteremia |
| Septic shock |

* *Mucositis is NOT a reason to add vancomycin if using cefepime monotherapy*

***If vancomycin is continued for >72hours and renal function remains stable, AUC monitoring should be used to minimize toxicity and maximize efficacy. Please contact ID pharmacy or ID for further assistance with this***

***If MRSA nares PCR is negative, recommend discontinuing empiric vancomycin unless other microbiologic evidence of MRSA or vancomycin susceptible Enterococcal infection***

****If blood cultures are positive for Gram positive organisms, particularly in pairs and chains, strongly consider daptomycin (+/- ampicillin) for empiric coverage of VRE. Contact ID for approval****

**5. Reevaluate at 48hr- need for escalation vs de-escalation of antibiotics:**

a. Patient is still **febrile:**
   - **i.** Have we found a **source**? Consider ID consult for further workup or possible antimicrobial adjustment

b. Patient is **afebrile but still neutropenic:**
   - i. If source found, narrow antibiotics to target the cultured organism and set a recommended course of duration
   - ii. If no source found and signs/symptoms of infection resolve after 3days of therapy, de-escalate back to levofloxacin prophylaxis until ANC >500 or monitor off antibiotics

c. Patient is **afebrile and no longer neutropenic:**
   - i. Stop antibiotics

**Management of select clinical syndromes as a cause of neutropenic fever:**

- Intra-abdominal infection suspected
  - Consider adding anaerobic coverage with metronidazole 500mg q12h or changing cefepime to piperacillin-tazobactam (adjusted for renal function)
  - If septic shock and intraabdominal source suspected, start meropenem + amikacin
  - Consider CT A/P
- *Clostridioides difficile* suspected
  - Send stool C diff test
  - Place patient in Contact (PLUS) isolation while test pending
  - Start patient on empiric PO vancomycin 125mg q6h or fidaxomicin 200mg q12h
    - Fidaxomicin is preferred for recurrent C diff
    - If concern for ileus / critically ill, begin PO vancomycin 500mg q6h + IV metronidazole and consult ID
- Meningitis/encephalitis suspected
  - Obtain imaging and LP – send CSF for cell count/diff, protein, glucose, bacterial culture, and meningitis-encephalitis panel (and other tests if clinically indicated)
  - In addition to cefepime, add IV vancomycin (dosed per nomogram), ampicillin 2g IV q4h, +/- IV acyclovir 10mg/kg q8h IBW
  - Obtain ID consult
- Respiratory viral illness suspected

    - Obtain SARS-CoV2/FLU/RSV
        - Place patient on special pathogen precautions while test pending
        - If positive for SARS-CoV2, consult ID for treatment recommendations and move patient to single room with special pathogen precautions if not already on isolation
        - If positive for influenza, start oseltamivir (renally dosed) and place patient in droplet isolation
            - If patient is in shared room, start prophylactic oseltamivir for roommate (ID approval needed)
    - If above tests are negative, consider respiratory viral panel
        - Place patient in droplet/contact isolation while test pending
- Pneumonia suspected
    - Send sputum culture, combined urine Legionella/Strep pneumo Ag
- Severe soft/tissue infection with concern for necrotizing fasciitis
    - Add clindamycin 900mg IV q8h
    - Consult surgery

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