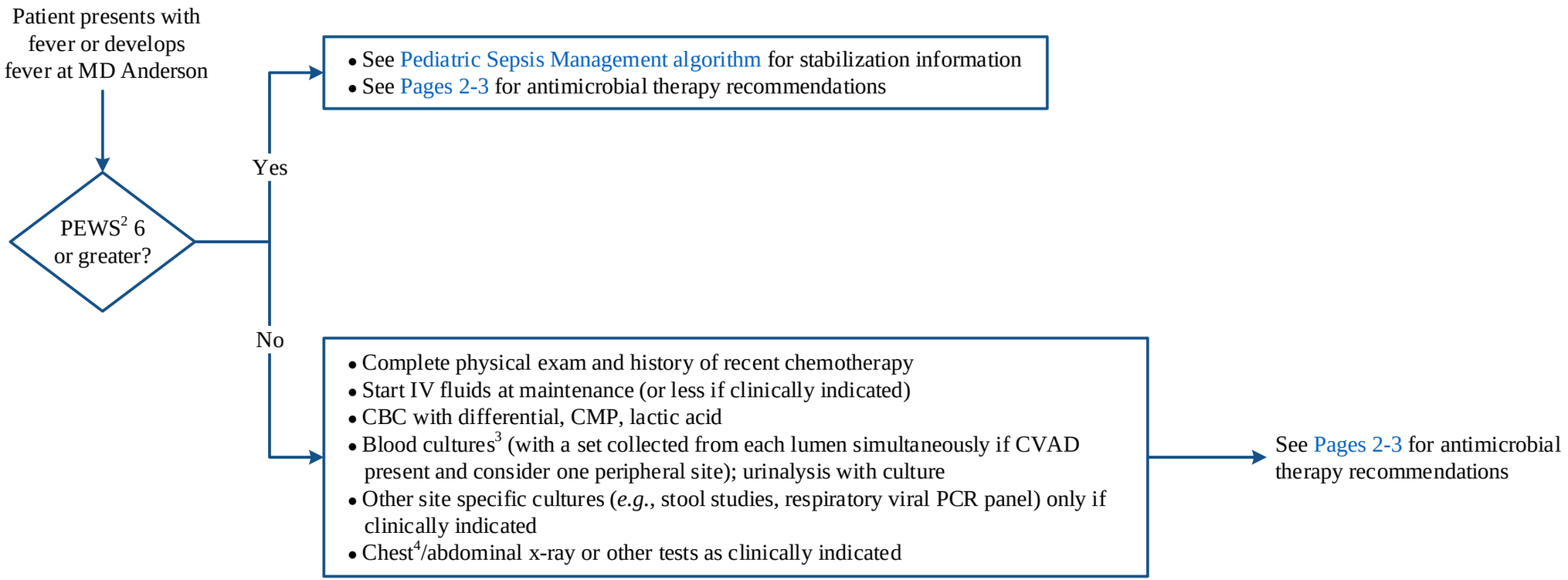
Neutropenic Fever[1] Inpatient Pediatric Treatment
(Hematologic Cancers and Stem Cell Patients)

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular toMD 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 not be used for patients receiving CAR cell therapy.



CAR = chimeric antigen receptor
CMP = comprehensive metabolic panel
CVAD = central venous access device
PEWS = Pediatric Early Warning Score

[1] ANC less than 1 K/microliter and either temperature of at least 38.3°C once or 38.0°C twice separated by at least 1 hour
[2] See Appendix A for Modified PEWS Tool; full details available in the Detecting Pediatric Patient Deterioration Using PEWS algorithm
[3] Do not delay antibiotic administration for blood cultures; antibiotics should be given within one hour
[4] Obtain chest x-ray for all stem cell transplant patients

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Consider the following when selecting antibiotics (antibiotics should be given within 1 hour):
- Recent culture and sensitivity results
- History of MDRO infection or colonization
- Suspected line infection[1]
- Antibiotic history and prophylaxis
- Source of infection if identified
- Antibiotic allergies
- Organ dysfunction
- Mucositis

Documented beta-lactam allergy (*i.e.*, hives or anaphylaxis)?

ANTIMICROBIAL THERAPY RECOMMENDATIONS
See Page 6 for Dosing Information

Gram negative coverage antibiotics should be given first

No

- **Neutropenic fever:**
  - Cefepime **or** piperacillin and tazobactam **or** meropenem[2]
- **If clinically suspected line infection[1], bacteremia, skin/soft tissue infection, MRSA colonization, and/or SCT patient:**
  - Add vancomycin
  - If relative contraindication exists to vancomycin use, consider linezolid[3] instead
- **If indicated for double gram negative coverage[4], add either:**
  - Tobramycin **or**
  - Amikacin **or**
  - Ciprofloxacin (only if no quinolone prophylaxis)
- **If mucositis (at least Grade 2), suspected intra-abdominal infection, or other indication for anaerobic coverage:**
  - Add metronidazole[5] to cefepime
- **If history of MDRO infection:**
  - Consider Infectious Disease consult

Yes

- **Neutropenic fever, clinically suspected line infection[1], bacteremia, skin/soft tissue infection, MRSA colonization, and/or SCT patient:**
  - Aztreonam[6]
- **Plus:**
  - Tobramycin **or** amikacin **or** ciprofloxacin (only if no quinolone prophylaxis)
- **Plus:**
  - Vancomycin
  - If relative contraindication exists to vancomycin use, consider linezolid[3] instead
- **If mucositis of at least Grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:**
  - Add metronidazole
- **If history of MDRO infection:**
  - Consider Infectious Disease consult

- See Page 3 for additional findings and antibiotic options
- See Page 4 for re-assessment

[1] Chills, rigors with infusion through catheter, cellulitis or discharge around the line entry site
[2] Consider meropenem if patient has any of the following:
- Non-IgE-mediated allergy to alternative agents
- Failed treatment with cefepime or piperacillin/tazobactam
- Infection with ESBL organism
- Infection with organism only susceptible to carbapenem

[3] Confirm use with Pediatric Stem Cell Transplant service prior to starting in transplant patients
[4] Double gram negative coverage should be considered with complicated tissue-based infections, neutropenic enterocolitis, and perirectal infections
[5] Metronidazole is not necessary if meropenem is used
[6] Double gram negative coverage recommended due to reduced aztreonam activity against gram negative organisms according to local MD Anderson antibiogram

ESBL = extended spectrum beta-lactamase
MDRO = multi-drug resistant organism
MRSA = methicillin-resistant *staphylococcus aureus*
SCT = stem cell transplant

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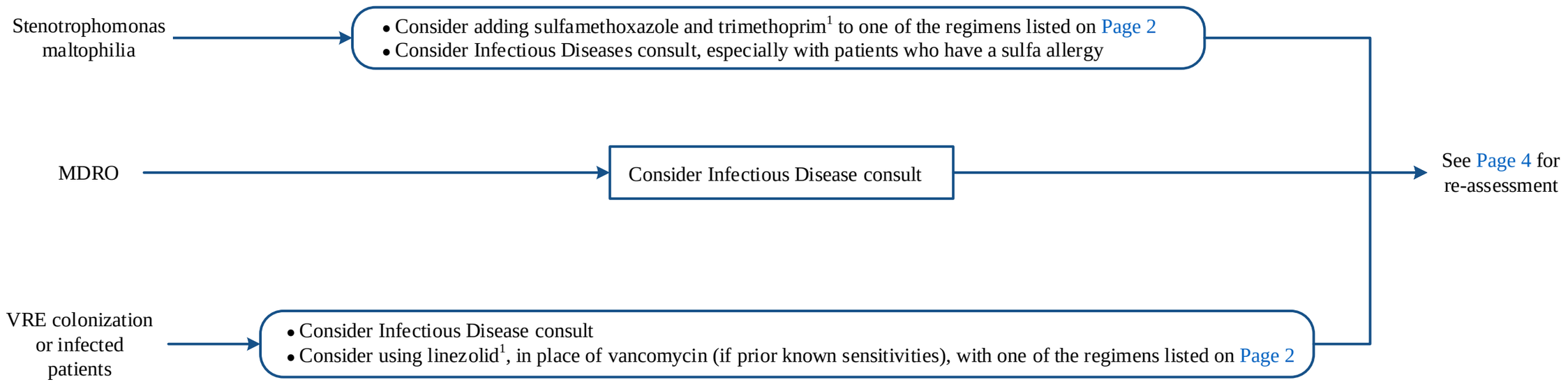
FINDINGS

ANTIMICROBIAL THERAPY RECOMMENDATIONS
See Page 6 for Dosing Information



VRE = vancomycin-resistant enterococci

[1] Confirm use with Pediatric Stem Cell Transplant service prior to starting in transplant patients

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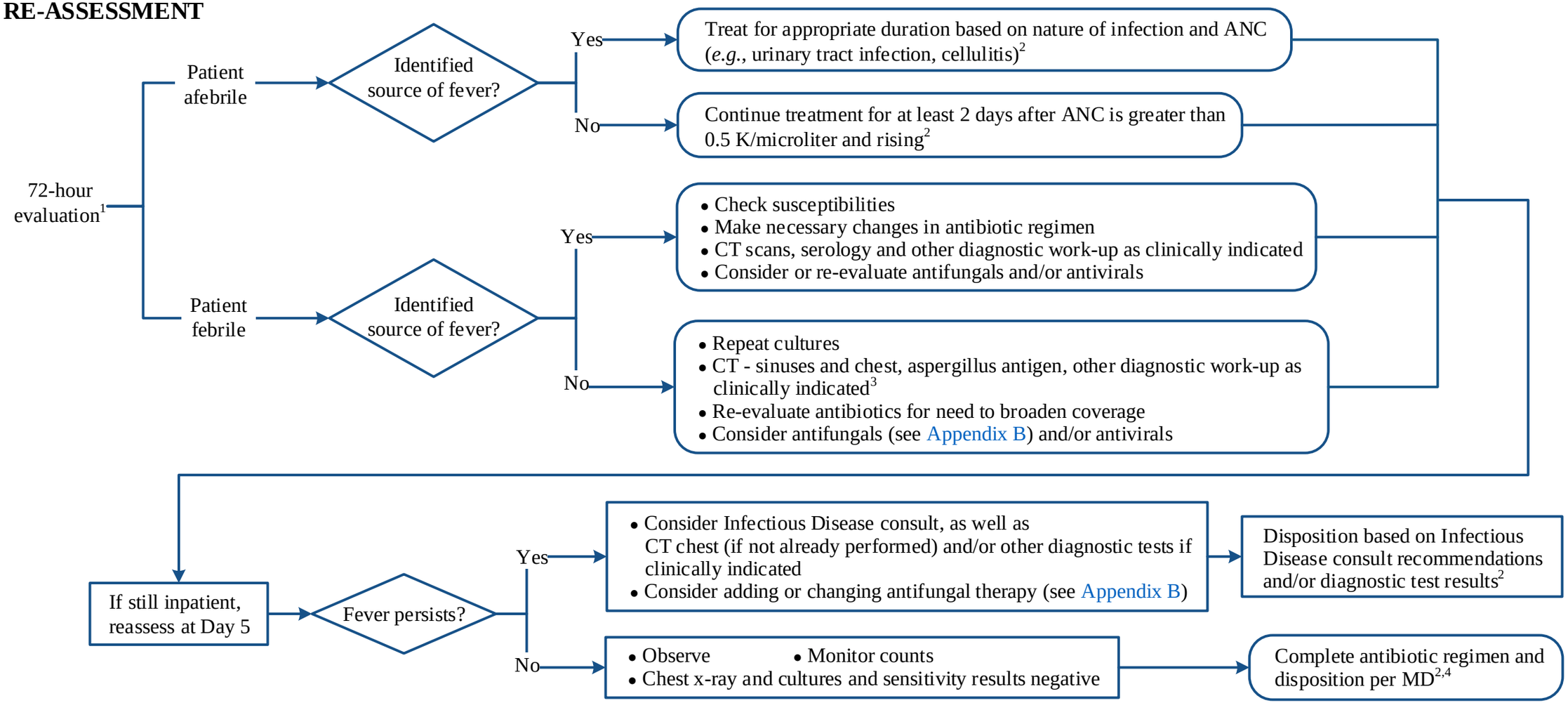
RE-ASSESSMENT



[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 or pneumonia)
[2] For stem cell patients, refer to the Stem Cell Transplantation and Cellular Therapy Guideline of Care GC14.2 for Febrile Neutropenia
[3] Cytomegalovirus (CMV) PCR for SCT patients if not already performed
[4] Consider transition to antimicrobial prophylaxis if otherwise indicated and no clear infectious source of fever was identified

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APPENDIX A: Modified PEWS Tool

	Score[1]			
	0	1	**2**	**3**
Behavior	• Playing • Appropriate	• Irritable, but consolable	• Irritated, but not consolable	• Lethargic • Confused • Reduced response to pain
Cardiovascular System				
Rate	• Within normal parameters for age	• Tachycardia less than 20 above normal for age	• Tachycardia 20-29 above normal for age	• Tachycardia at least 30 above **or** bradycardia at least 10 below normal for age
Color	• Pink	• Pale **or** dusky	• Mottled	• Gray
Perfusion	• Capillary refill 1-2 seconds	• Capillary refill 3 seconds	• Capillary refill 4 seconds	• Capillary refill at least 5 seconds
Respiratory System				
Rate	• Within normal parameters for age	• Tachypnea 10-19 above normal parameters for age	• Tachypnea at least 20 above normal parameters for age with retractions	• Bradypnea at least 5 below normal parameters for age with retractions
Effort	• No retractions	• Mild retractions/accessory muscle use	• Moderate retractions/accessory muscle use (including tracheal tugging)	• Severe retractions/accessory muscle use (including tracheal tugging) **and** grunting
Oxygen	• N/A	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 24-40% ◦ 2 L/minute O_2 • Any assisted ventilation[3] or initiation of O_2	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 40-49% ◦ At least 3 L/minute O_2	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 of at least 50%

[1] Add 2 extra points if patient requires frequent interventions (*e.g.*, suctioning, positioning, change in O_2 needs, multiple IV attempts required, or every 15-minute or continuous nebulized treatments) or has persistent post-op vomiting
[2] As defined in patient's orders
[3] Includes home bilevel positive airway pressure (BiPAP)/continous positive airway pressure (CPAP) or home ventilator at baseline settings

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APPENDIX B: Antimicrobial Dosing Information

Note: Adjust dose for patients with renal/hepatic dysfunction. Therapeutic drug monitoring should be performed to ensure safety and efficacy, as appropriate.

Antibiotic agents:

- Amikacin 15 mg/kg IV once and then repeat per pharmacokinetic data
- Aztreonam 30 mg/kg (maximum 2 g) IV every 8 hours
- Cefepime 50 mg/kg (maximum 2 g) IV every 8 hours
- Ciprofloxacin 10 mg/kg (maximum 400 mg) IV every 8 hours
- Linezolid[1]
  - Less than 12 years old: 10 mg/kg (maximum 600 mg) IV every 8 hours
  - Greater than or equal to 12 years old: 600 mg IV every 12 hours
- Meropenem 20 mg/kg (maximum 1 gram) IV every 8 hours
- Metronidazole 7.5 mg/kg (maximum 500 mg) IV every 6 hours
- Piperacillin and tazobactam 100 mg/kg piperacillin (maximum 4 grams) IV every 8 hours
- Sulfamethoxazole and trimethoprim (TMP)[1] 5 mg/kg TMP IV or oral every 8 hours
- Tobramycin 7 mg/kg IV once and then repeat per pharmacokinetic data
- Vancomycin
  - Less than 6 years old: 20 mg/kg IV every 6 hours
  - 6-11 years old: 15 mg/kg IV every 6 hours
  - Greater than 11 years old: 15 mg/kg IV every 8 hours

Antifungal agents:

- Caspofungin - load 70 mg/m^2 (maximum 70 mg) IV once, then 50 mg/m^2 (maximum 50 mg) IV daily
- Liposomal Amphotericin 3-5 mg/kg IV daily
- Voriconazole
  - Patients 2 to 11 years old:
    - Loading dose: 9 mg/kg/dose IV every 12 hours x 2 doses
    - Maintenance dose: 8 mg/kg/dose IV every 12 hours
  - Patients greater than or equal to 12 years old:
    - Loading dose: 6 mg/kg/dose IV every 12 hours x 2 doses
    - Maintenance dose: 4 mg/kg/dose IV every 12 hours

[1] Confirm use with Pediatric Stem Cell Transplant service prior to starting

SUGGESTED READINGS

Freifeld, A. G., Bow, E. J., Sepkowitz, K. A., Boeckh, M. J., Ito, J. I., Mullen, C. A., . . . Wingard, J., R. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, *52*(4), e56-e93. doi:10.1093/cid/cir073

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DEVELOPMENT CREDITS

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

Patricia Amado, BSN, RN (Nursing G9)
Natalie J.M. Dailey Garnes, MD (Infectious Disease)[Ŧ]
Jessica Foglesong, MD (Pediatrics – Patient Care)
Suzanne Gettys, PharmD (Pharmacy Clinical Programs)
Kris Mahadeo, MD (Pediatrics – Patient Care)
Victor Mulanovich, MD (Infectious Disease)
Demetrios Petropoulos, MD (Pediatrics – Patient Care)
Shehla Razvi, MD (Pediatrics – Patient Care)[Ŧ]
Milena Zhang, PharmD[♦]

[Ŧ] Core Development Team Lead
[♦] Clinical Effectiveness Development Team