MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

GUIDELINES FOR TREATMENT OF BONE AND JOINT INFECTIONS IN ADULTS

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Revision History:
02/2021: Added fungi, mycobacteria, and Actinomyces comment
03/2021: Updated vancomycin dosing & hyperlinks
09/2021: Updated vancomycin infusion reaction terminology
08/2023: Added oral antibiotics section, major revisions to pelvic, diabetic foot, prosthetic joint sections, new beta-lactam allergy comments

Oral Antibiotics in the Treatment of Osteomyelitis

- **Given nuances in dosing and decision-making, recommend ID consultation**
- **Rationale:**
  - Randomized control trials in osteomyelitis as well as observational clinical data show that oral therapy leads to similar clinical success as intravenous therapy.
  - Central venous catheters and long-term intravenous antibiotic therapy carry numerous risks for vascular access complications, CVC-associated venous thrombosis, adverse drug events.
- **Patient Selection Criteria:**
  1. Clinically stable (hemodynamically stable, and stable at the site of infection, e.g., no spinal instability)
  2. Adequate source control (i.e., not requiring drainage, no persistent bacteremia)
  3. Able to absorb oral medications from a functioning GI tract.
  4. Have an available regimen used in published studies to cover likely target pathogens (see regimens below).
  5. Have no psychosocial reasons that preclude the safe use of oral therapy.

Antimicrobial	**Recommended Dose (CrCl > 50 mL/min, 70 kg)**	**Adverse effects**	**Comments**
Amoxicillin-clavulanate	875 mg-125 mg PO BID OR up to TID	Diarrhea, hypersensitivity reactions	Data mainly in diabetic foot osteomyelitis. Consider alternative options in patients with obesity, and for the treatment of prosthetic joint infections or vertebral osteomyelitis.
Cephalexin	1 g PO TID OR up to QID	Hypersensitivity reactions	Limited data in adult osteomyelitis, consider use in culture-guided therapy with good debridement. Consider alternative options in patients with obesity, and for the treatment of prosthetic joint infections or vertebral osteomyelitis.
Ciprofloxacin*	750 mg PO BID	Tendinopathy, *C. difficile.* Ciprofloxacin has minimal to no effect on Qtc	Robust RCT data in osteomyelitis.
Clindamycin	600 mg PO TID OR 450 mg PO QID	*C.difficile* colitis	Increasing MRSA resistance to Clindamycin.
Doxycycline	100 mg PO BID	GI upset, photosensitivity, esophagitis	Less published data in OM, has been used with anecdotal success and was used in a minority of patients in the OVIVA trial.
Levofloxacin*	750 mg PO daily	Prolonged Qtc, tendinopathy, *C. difficile*	Robust RCT data in osteomyelitis.
Linezolid	600 mg PO BID	Thrombocytopenia after 2 weeks. Long term: neuropathy, including optic neuritis.	Contraindicated in patients on MAO-I. Can be used, with caution, in pts on other serotonergic agents: SSRI & Linezolid Education. Consider monitoring of platelet counts for longer duration. To monitor Linezolid levels, talk with ID pharmacy.
Metronidazole	500 mg PO BID	Nausea, neuropathy	Anaerobic coverage is not routinely needed, consider if the wound is gangrenous or there is specific concern for anaerobic infection. Twice daily dosing is sufficient for definitive treatment of most anaerobic infections.
Minocycline	100 mg PO BID	GI upset, photosensitivity, esophagitis	Less published data in OM. Use 200 mg BID for *Stenotrophomonas/Acinetobacter*
Rifampin	600 mg PO daily	Significant drug-drug interactions, often not feasible	Given in addition to other agents (including FQ) to treat *S aureus* PJI for biofilm activity. Should only be given in addition to fluoroquinolones in PJI as a biofilm-active agent for Staph aureus
Trimethoprim/ Sulfamethoxazole	7.5-10 TMP mg/kg/day PO divided BID or TID (e.g., 2 DS tablets PO BID for a 70 kg adult)	AKI, hyperkalemia, hypersensitivity	Strongly consider alternative therapy or close lab monitoring in patients with concomitant ACE/ARB and/or potassium-sparing diuretic administration

*Avoid fluoroquinolone monotherapy in *Staphylococcus aureus* OM given high rate of relapse

Hematogenous Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually associated with: • Patients under age 17 years or over 50 years (recommendations intended for adults only) • injection drug use • Other risk for bacteremia e.g., central line, dialysis, sickle cell disease, urethral catheterization, UTI Bacterial Etiology: • *S. aureus* • 30% Gram negative bacilli (consider if fresh water exposure, recent broad spectrum antibiotics in the prior 90 days, recent >2 days hospitalized in prior 90 days, or hemodynamic instability) • *Salmonella* in sickle cell disease • *Serratia* and *Pseudomonas spp*. in injection drug use	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) If known MSSA colonization or infection: **Cefazolin*** 2 g IV q8h Alternative for vancomycin allergy (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily If Sickle Cell disease: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 2 g IV daily If injection drug use or other Gram negative risk (see bacterial etiology) OR Alternative for patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) + **Piperacillin-tazobactam** 4.5 g IV q6h If injection drug use or other Gram-negative risk (see bacterial etiology); OR Alternative for patient with low- to high-risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime** 2 g IV q8h Alternative for patients with non Ig-E mediated beta-lactam allergy (e.g., DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem** 2 g IV q8h	4-6 weeks *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.*	Approximately 45% of *S. aureus* at Michigan Medicine are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if methicillin-susceptible *S. aureus* (MSSA) is identified. Infectious Diseases Consultation recommended. **Daptomycin** requires prior approval. Baseline CK followed by weekly CK should be measured in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Increased dose of **daptomycin** may be indicated with documented MRSA bacteremia. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Vertebral Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually hematogenous source Persons at risk: • Age > 60 years • Injection drug use • Urinary tract infections Bacterial Etiology: • *S. aureus* • Occ. Coagulase negative *staphylococcus* • Enteric Gram negatives • *Pseudomonas* in injection drug use or water exposure	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 2 g IV q12h If known MSSA colonization or infection: **Oxacillin** 2 g IV q4h Alternative for suspected or documented Pseudomonal infection (see bacterial etiology); OR Patient with low- to high-risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for patients with non-Ig-E mediated beta-lactam allergy (e.g. DRESS, SJS, TENS) or cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem*** 2 g IV q9h Alternative for vancomycin allergy or intolerance (not vancomycin infusion reaction**): **Linezolid** 600 mg PO/IV q12h + other antibiotic as indicated above	6 weeks if all abscesses are drained with surgery or interventional radiology Consider longer duration (e.g., 8 weeks) of antibiotics for patients at high risk of recurrence – i.e., MRSA infection, undrained abscess, ESRD *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.*	Evaluation for epidural infection is critical. See full Vertebral Osteomyelitis FGP Guideline Infectious Diseases consultation strongly recommended. Approximately 45% of *S. aureus* at Michigan Medicine are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. Empiric dosing and agent selection takes into account epidural abscess with possible CNS extension. The need for **CNS coverage in the definitive regimen depends on whether epidural extension was found on workup and whether or not there was surgical intervention.** If oral therapy is considered, recommend agents with high oral bioavailability, e.g., linezolid, fluoroquinolones. **Cefazolin** may replace **oxacillin** if no epidural extension of infection is present. **Daptomycin** may replace **linezolid** if no epidural extension of infection is present. **Linezolid** requires prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** is contraindicated in patients on MAO-I. It can be used, with caution, in pts on other serotonergic agents. See SSRI & Linezolid Education. **Daptomycin** may replace **linezolid** if no epidural extension of infection is present. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Native Joint Septic Arthritis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Usually associated with: • Age >80 years • Diabetes mellitus • Rheumatoid arthritis • Skin infection • Injection drug use • Alcohol use disorder • Prior intra-articular steroid injection Bacterial Etiology: • *S. aureus* • Streptococcal species, including *S. pneumoniae* • Gram negative bacilli associated with trauma, intravenous drug users, older adults, and in association with underlying immunosuppression. • *N. gonorrhea* in oligoarthritis, (particularly young, sexually active), associated tenosynovitis, vesicular pustules, late complement deficiency, negative synovial fluid culture and Gram stain	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred: **Vancomycin*** IV (see nomogram) If known MSSA colonization or infection: **Cefazolin*** 2 g IV q8h Alternative for vancomycin allergy (not vancomycin infusion reaction**): **Linezolid** 600 mg PO/IV q12h OR **Daptomycin*** 6 mg/kg IV daily If risk for gonorrhea: **Vancomycin*** IV (see nomogram) + **Ceftriaxone** 1 g IV daily + **Azithromycin** 1 g PO in a single dose If risk for Gram negative bacilli (see bacterial etiology) OR Alternative for patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for patient with low- to high-risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime** 2 g IV q8h Alternative for patients with non-Ig-E mediated beta-lactam allergy (e.g. DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem** 2 g IV q8h	2-4 weeks Small joint (i.e., finger) infections following surgical debridement/washout: Consider 2 weeks For *S. aureus* (esp large joints): Minimum 4 weeks For *N. gonorrhea*: After 24-48h of ceftriaxone with substantial clinical improvement, transition to oral stepdown therapy to complete total of at least 7 days *Consider oral therapy for part of the duration in the appropriate patient.*	Approximately 45% of *S. aureus* at Michigan Medicine are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. Consult Orthopedic surgery for joint drainage. ID consultation recommended. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** is contraindicated in patients on MAO-I. It can be used, with caution, in pts on other serotonergic agents. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be measured in patients placed on **Daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Pelvic Osteomyelitis Underlying Pressure Ulcers			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Osteomyelitis underlying pressure ulcer Bacterial Etiology: Mixed infections due to *Staphylococcus sp., Streptococcus sp.* and enteric organisms	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred; can be used in patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for patient with low to high-risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime** 2 g IV q8h **+ Metronidazole** 500 mg PO/IV q8h Alternative for patients with non Ig-E mediated beta-lactam allergy (e.g., DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem** 2 g IV q8h Alternatives for vancomycin intolerance (not vancomycin infusion reaction**) or allergy: **Daptomycin*** 6 mg/kg IV daily + other antibiotic as indicated above.	Acute osteomyelitis (not previously treated), or chronic osteomyelitis following surgical debridement and flap coverage with positive intraoperative cultures: 6-8 weeks Acute skin and soft tissue infection or flare of symptoms from wound following initial 6-8 week course of treatment: Consider 7-14 days in appropriate patients *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.*	There is no data to demonstrate that long term antibiotic therapy in clinically stable patients without an operative plan for tissue coverage setting improves healing or reduces recurrence of ulcers. Multidisciplinary management recommended: consider consult to ID, plastic surgery or wound care, orthopedic surgery, physical medicine and rehabilitation, colorectal surgery, urology, nutrition. This may be done as an outpatient in hemodynamically stable patients. Other important components of management include pressure offloading, nutritional optimization, smoking cessation, consideration of diversion colostomy/urostomy. Tailor therapy based on culture data. Treatment should be modified to cover previously isolated pathogens with recurrent or relapse of the same site. **Daptomycin** requires prior approval. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Diabetic Foot Infection/Osteomyelitis			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Patient presenting with acute diabetic foot infection/OM without risk factor for GNR infection (see below) Microbiology: • Staphylococcus spp (esp *S. aureus*) • *Streptococcus* spp • *Corynebacterium* and other skin flora	**Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients** Preferred: **Vancomycin*** IV (see nomogram) Alternatives for Vancomycin intolerance (not vancomycin infusion reaction**) or allergy: **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg PO/IV q12h	Non-operative management: 6 weeks Debridement with active osteomyelitis at margins (not curative amputation): 3-6 weeks* Total resection with clean margins (i.e. below-knee amputation) ≤ 2-5 days post-op. *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.*	Surgical debridement of overlying ulcer with deep tissue or bone biopsy is an important component of management. Multidisciplinary management recommended: consider consult to ID, podiatry; to vascular surgery/orthopedic surgery, physical medicine and rehabilitation as appropriate. Other important components of management include offloading, glycemic control, smoking cessation, management of concurrent foot pathology. Tailor therapy based on culture data. In small RCTs, 3 week duration of antibiotics was noninferior to 6 weeks for patients following surgical debridement[12] Treatment should be modified to cover previously isolated pathogens with recurrent or relapse of the same site. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** is contraindicated in patients on MAO-I. It can be used, with caution, in pts on other serotonergic agents. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.
Anti-Pseudomonal gram negative coverage is indicated in these patients: • Recurrent/relapsed infection • Previously isolated gram-negative pathogen • Fresh water exposure • Broad spectrum antibiotics in the prior 90 days • recent >2 days hospitalized in prior 90 days hemodynamic instability	Preferred; can be used in patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for patient with low to high risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime** 2 g IV q8h + **Metronidazole** 500 mg PO/IV q8h Alternative for patients with non Ig-E mediated beta-lactam allergy (e.g., DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem** 2 g IV q8h Alternatives for Vancomycin intolerance (not vancomycin infusion reaction**) or allergy **Daptomycin*** 6mg/kg IV daily OR **Linezolid** 600mg PO/IV q12h + other antibiotic as indicated above.		

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Prosthetic Joint infection

Clinical Setting	Empiric Therapy	Duration	Comments
Higher risk associated with: • Prior arthroplasty • Rheumatoid arthritis • Perioperative infection • Prior joint infection • Prolonged surgery • High BMI • Postoperative bleeding • Diabetes mellitus • Advanced age Bacterial Etiology: Early onset: <3 months after surgery • *S. aureus* • Aerobic Gram negative bacilli • Anaerobes • Mixed infections Delayed onset: 3-24 months after surgery • Coagulase negative *Staphylococcus* • *Enterococcus* • *Cutibacterium* Late onset: >24 months after surgery • *S. aureus* • Beta-hemolytic *Streptococci* • Aerobic Gram negative bacilli	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients *Early (< 3 mo) and Late (> 24 mo) Onset* Preferred; can be used in patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) + **Piperacillin-tazobactam** 4.5 g IV q6h Suspected/Documented Gram negative Infection OR Alternative for patient with low to high risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for patients with non Ig-E mediated beta-lactam allergy (e.g., DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Meropenem*** 2 g IV q8h Alternative for Vancomycin Allergy or Intolerance (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg PO/IV q12h + other antibiotic as indicated above *Delayed (3-24 mo) Onset* Preferred: **Vancomycin*** IV (see nomogram)	PJI with debridement, antibiotics, and implant retention (DAIR): 12 weeks, esp in *S. aureus** PJI with 1-stage exchange, non-*S. aureus* pathogens: 6 weeks* 2 stage exchange: 6 - 12 weeks* *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.* *Antimicrobial Suppression may be considered in some cases of retained hardware.*	Infectious Diseases consultation strongly recommended. *Based on DATIPO RCT, 12 weeks is preferred to 6 weeks of antibiotics for PJI treated with DAIR. For PJI treated with prosthetic exchanges, some believe equipoise remains between 6 vs 12 weeks, particularly *if S aureus* is not the etiologic pathogen, or for 1-stage exchanges or 2-stage revisions with negative cultures prior to implantation Most common oral antibiotics used in DATIPO RCT: Fluoroquinolones (~70%) +/- rifampin (~70%), and clindamycin (~23%). Less frequently used: amoxicillin/clavulanate (10%), TMP/SMX (15%) In DATIPO RCT, relapse rates for PJI after all antibiotic were stopped at 12 weeks was 8%, even with retained hardware. Approximately 45% of *S. aureus* at Michigan Medicine are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if methicillin-susceptible *S. aureus* (MSSA) is identified. Consider addition of rifampin in the setting of new hardware placement especially in *S aureus* infections. If rifampin use is being considered, it may be prudent to wait until bacteremia is cleared (if present) and surgical source control is achieved (if necessary), to reduce the risk of treatment failure. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** is contraindicated in patients on MAO-I. It can be used, with caution, in pts on other serotonergic agents. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

Osteomyelitis following Trauma and/or Orthopedic Procedures			
Clinical Setting	**Empiric Therapy**	**Duration**	**Comments**
Associated with contaminated open fractures or surgical treatment of closed fractures Bacterial Etiology: Most common • *S. aureus* • Coagulase negative *Staphylococcus* • Enteric Gram-negative bacilli Less common • *Enterococcus sp.* • *Acinetobacter* • *Pseudomonas sp.* • Anaerobes	Consider holding antibiotics until deep tissue cultures can be obtained in hemodynamically stable patients Preferred; can be used in patients with low-risk cephalosporin allergy: **Vancomycin*** IV (see nomogram) **+ Piperacillin-tazobactam*** 4.5 g IV q6h Alternative for Vancomycin Allergy or Intolerance (not vancomycin infusion reaction**): **Daptomycin*** 6 mg/kg IV daily OR **Linezolid** 600 mg IV q12h **+** other antibiotic as indicated above. Alternative for patient with low to high risk penicillin allergy (including anaphylaxis): **Vancomycin*** IV (see nomogram) + **Cefepime*** 2 g IV q8h Alternative for patients with non Ig-E mediated beta-lactam allergy (e.g. DRESS, SJS, TENS) or high-risk cephalosporin allergy: **Vancomycin*** (see nomogram) **+ Meropenem** * 2 g IV q8h	Total resection with clean margins (i.e., below-knee amputation): ≤ 2-5 days post-op Acute osteomyelitis at margins (not curative amputation): 6 weeks *Consider oral therapy for part of the duration in the appropriate patient. See Patient Selection Criteria on page 2.* *Antimicrobial suppression may be considered in some cases of retained hardware.*	Infectious Diseases consult strongly recommended. Approximately 45% of *S. aureus* at Michigan Medicine are MRSA, so initial treatment to cover MRSA is warranted. De-escalate to a beta-lactam if *methicillin-susceptible S. aureus (MSSA)* is identified. **Linezolid** and **daptomycin** require prior approval. Baseline CBCP and weekly CBCP are recommended with **linezolid** therapy due to risk of cytopenia, especially thrombocytopenia; alternative therapy should be considered in patients with thrombocytopenia. **Linezolid** is contraindicated in patients on MAO-I. It can be used, with caution, in pts on other serotonergic agents. See SSRI & Linezolid Education. Baseline CK followed by weekly CK should be followed in patients placed on **daptomycin** due to increased risk of rhabdomyolysis. Infections due to fungi, mycobacteria, or *Actinomyces* require longer durations of therapy – consult appropriate national guidelines for guidance. For beta-lactam risk categories and further guidance see the B-lactam allergy guideline.

* Adjust dose based on renal function; vancomycin dose may require adjustment for select organisms or patients
Target vancomycin AUC 400-600 mcg*hr/mL

** For vancomycin infusion reactions, vancomycin infusion should be slowed to > 2 hr

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