University of Nebraska Medical Center
Nebraska Medicine

UNMC Criteria for Appropriate Use of OPAT in Bone and Joint Infections

Early use of oral antibiotics for bone and joint infections, including complex orthopedic device-related infections, is well-grounded in clinical trial data demonstrating equivalent efficacy with improved safety[1-7], as well as in society guidances[8-12], and peer institutional policies[13-14]. To promote both patient safety and high-value care, the UNMC Outpatient Parenteral Antimicrobial Therapy (OPAT) team has chosen to institute basic appropriate use criteria for orthopedic infections. *ID clinicians who want to use IV antibiotics outside of these criteria will need to independently coordinate and oversee this care.*

Please note that the following criteria are intended as a *floor* for appropriate use and include several patient subpopulations who available evidence indicates are at elevated risk of treatment failure, but for which there is little to no evidence indicating that said risk is mitigated with parenteral versus oral therapy. These criteria are intended as a generous definition of patients in whom prolonged parenteral therapy *may* be reasonable. For many patients meeting these criteria, however, oral antimicrobial therapy under ID specialist supervision often remains an appropriate and evidence-based strategy.

As of July 1, 2026, OPAT team coordination for bone and joint infections at UNMC will be limited to patients with:

- Orthopedic device infections that are either recurrent or being managed with DAIR (implant retention)
- Vertebral osteomyelitis
- Concurrent infective endocarditis
- Concurrent *S. aureus* bacteremia (within the first two weeks of culture clearance)
- Unhoused status or active/prohibitive substance use disorder (when dalbavancin is requested to ensure treatment adherence)
- Early postoperative discharge, when operative culture results are still pending (i.e. operative culture results at 48hr are not yet reported)
- Enteral malabsorption requiring TPN/PPN or intractable nausea/vomiting
- Infection due to a pathogen for which all highly bioavailable oral options (see list at the end of this document) are strictly contraindicated, defined as:
    - Organism resistant to candidate oral antibiotic

- Severe allergy to candidate oral antibiotic (history of non-severe PCN allergy should be interrogated during hospitalization)
- Documented prior intolerance of the candidate oral antibiotic
- Prohibitive interaction between candidate oral antibiotic and patient-specific factors, including:
  - (for TMP/SMX) CrCl <30 mL/min
  - (for linezolid) Concurrent serotonergic therapy with either ≥2 other agents, or with (es)citalopram [Celexa/Lexapro], or intended treatment duration ≥4 weeks
  - (for levofloxacin and moxifloxacin) Pretreatment QTc >500 or co-administration of other QT-prolonging agents
  - (for all fluoroquinolones) History of collagen-vascular disease, including prior tendon rupture, retinal detachment, or vascular aneurysm

Implementation guidance:

- For patients with a bone and joint infection who receive an OPAT consult but do not meet these criteria, the OPAT team will communicate that to the ID team's attending physician via PerfectServe along with a specific oral antibiotic recommendation
- An attending who wants to prescribe IV antibiotics outside of these criteria will be responsible for coordinating all aspects of OPAT with the patient's RN/care transition nurse/case manager, and will also be responsible for subsequent OPAT oversight. Responsibilities include (but are not limited to) ensuring central line is placed, ensuring infusion pharmacies receive appropriate orders for antimicrobials and associated safety labs, obtaining and reviewing lab results, being the point of contact to triage potential adverse events, ensuring central lines are removed or line care is handed-off if it is to be retained for non-ID indications, and contacting patients who do not attend their ID clinic follow-up appointment.
- When an attending prescribes IV antibiotics outside of these criteria and takes responsibility for safety monitoring of the patient during OPAT, *this responsibility remains with the prescribing attending until the patient is seen in ID clinic by another provider*. Attendings who would like their patients to switch to oral antibiotics earlier but do not have ID clinic availability are encouraged to schedule an off-template appointment either in person or via telehealth, through the ID nursing team.

Regimens recommended for oral therapy conversion when encountering *culture-negative* bone and joint infections

Note: Regimens not necessarily listed in order of preference/recommendation – patient-specific factors will likely most inform the preferable choices

Infections associated with orthopedic hardware (e.g. prosthetic joint or fracture-related infections)

Rationale: Orthopedic device-related infections are most commonly related to coagulase-negative staphylococci and particularly MRSE (for which tetracyclines and linezolid are the most reliable oral therapies at our institution), followed by S. aureus, non-pseudomonal GNRs, and streptococci.[15-16] Minocycline is generally preferred over doxycycline due to modestly higher susceptibilities among S. epidermidis, but doxycycline is an acceptable alternative.

- Minocycline/doxycycline + fluoroquinolone
- Linezolid + fluoroquinolone (can be considered to complete treatment when only a few weeks of therapy remain)
- Minocycline/doxycycline + amoxicillin-clavulanate (can be considered, but with a lower body of evidence specifically in device-related infection)

Infections not associated with orthopedic hardware (e.g. diabetes-related foot osteomyelitis (DFO) and native joint septic arthritis)

Rationale: S. aureus (primarily MSSA), streptococci, non-pseudomonal GNRs, and anaerobes predominate in diabetes-related foot infections in our region. For other forms of native osteoarticular infection, anaerobes are less prevalent but the microbiology is otherwise similar.

- Regimens Specifically for DFO
  - Doxycycline/minocycline + amoxicillin-clavulanate
  - Trimethoprim-sulfamethoxazole + amoxicillin-clavulanate
  - Linezolid + fluoroquinolone +/- metronidazole (Can be considered to complete treatment when only a few weeks of therapy remain. Metronidazole may be superfluous, particularly when source control has been adequate and the patient has had substantial lead-in with anti-anaerobic therapy.)
- Doxycycline/minocycline + cefadroxil
- Doxycycline/minocycline + fluoroquinolone
- Trimethoprim-sulfamethoxazole

Oral antibiotic dosing recommended for most cases of bone/joint infections (assuming no dose adjustments necessary for organ dysfunction)

- Amoxicillin 1g q8h
- Amoxicillin-clavulanate 875/125mg q8-12hr
- Cefadroxil 1g q12h
- Cephalexin 1g q8h
- Ciprofloxacin 750mg q12h
- Doxycycline 100mg q12h

- Fluconazole (isolates with MIC ≤4)
  - TBW 60-89kg: 400mg daily
  - TBW 90-120kg: 600mg daily
- Levofloxacin 750mg daily
- Linezolid 600mg q12h (for courses >2wks, consult COpAT and utilize TDM)
- Minocycline 100mg q12h
- Rifampin 600mg daily
- Trimethoprim-sulfamethoxazole (for courses >2-3wks, consider COpAT consult)
  - AdjBW 40-69kg: 1 DS tab q12h
  - AdjBW 70-100kg: 2 DS tab q12h

Developed by Nicolas Cortes-Penfield, MD; Bryan Alexander, PharmD; Molly Miller, PharmD; Sara Azimi, PharmD

Reviewed and Approved by Antimicrobial Stewardship Committee: August 2026

REFERENCES

2. Li HK, Rombach I, Zambellas R, Walker AS, McNally MA, Atkins BL, et al; OVIVA Trial Collaborators. Oral versus Intravenous Antibiotics for Bone and Joint Infection. N Engl J Med. 2019 Jan 31;380(5):425-436. doi: 10.1056/NEJMoa1710926. PMID: 30699315;
3. Manning L, Metcalf S, Dymock M, Robinson O, Clark B, Nelson R, et al; Australasian Society for Infectious Diseases Clinical Research Network. Short- versus standard-course intravenous antibiotics for peri-prosthetic joint infections managed with debridement and implant retention: a randomised pilot trial using a desirability of outcome ranking (DOOR) endpoint. Int J Antimicrob Agents. 2022 Jul;60(1):106598. doi: 10.1016/j.ijantimicag.2022.106598. Epub 2022 May 6. PMID: 35533791.
3. Major Extremity Trauma Research Consortium (METRC); Obremskey WT, O'Toole RV, Morshed S, Tornetta P 3rd, Murray CK, Jones CB, et al. Oral vs Intravenous Antibiotics for Fracture-Related Infections: The POvIV Randomized Clinical Trial. JAMA Surg. 2025 Jan 22. doi: 10.1001/jamasurg.2024.6439. Epub ahead of print. PMID: 39841468.
5. Juskowich JJ, Thompson JM, Bage SD, Palmateer KM, Guilfoose JA, Lastinger AM, et al. Using the Comparing Oral versus Parenteral Antimicrobial Therapy (COPAT) Clinical Trial to Influence Institutional Practice Transformation Towards Earlier Transition to Oral Antibiotics. Clin Infect Dis. 2026 Apr 30;82(4):e674-e681. doi: 10.1093/cid/ciaf707. PMID: 41419216;
6. Nielsen AB, Holm M, Lindhard MS, Glenthøj JP, Borch L, Hartling U, et al. Oral versus intravenous empirical antibiotics in children and adolescents with uncomplicated bone and joint infections: a nationwide, randomised, controlled, non-inferiority trial in Denmark. Lancet Child Adolesc Health. 2024 Sep;8(9):625-635. doi: 10.1016/S2352-4642(24)00133-0. Epub 2024 Jul 15. PMID: 39025092.

7. Davar K, Clark D, Centor RM, Dominguez F, Ghanem B, Lee R, et al. Can the Future of ID Escape the Inertial Dogma of Its Past? The Exemplars of Shorter Is Better and Oral Is the New IV. Open Forum Infect Dis. 2022 Dec 29;10(1):ofac706. doi: 10.1093/ofid/ofac706. PMID: 36694838; Cortés-Penfield NW, Justo JA, McCreary EK, Ryder JH. Optimizing Antibiotic Therapy in Musculoskeletal Infections. Infect Dis Clin North Am. 2025 Sep;39(3):361-382. doi: 10.1016/j.idc.2025.02.009. Epub 2025 Apr 11. PMID: 40221230.

8. Senneville É, Albalawi Z, van Asten SA, Abbas ZG, Allison G, Aragón-Sánchez J, Embil JM, Lavery LA, Alhasan M, Oz O, Uçkay I, Urbančič-Rovan V, Xu ZR, Peters EJG. IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023). Clin Infect Dis. 2023 Oct 2:ciad527. doi: 10.1093/cid/ciad527. Epub ahead of print. Erratum in: Clin Infect Dis. 2024 Jul 19;79(1):286. doi: 10.1093/cid/ciae287. PMID: 37779457.

10. Spellberg B, Aggrey G, Brennan MB, Footer B, Forrest G, Hamilton F, et al; WikiGuidelines Group. Use of Novel Strategies to Develop Guidelines for Management of Pyogenic Osteomyelitis in Adults: A WikiGuidelines Group Consensus Statement. JAMA Netw Open. 2022 May 2;5(5):e2211321. doi: 10.1001/jamanetworkopen.2022.11321. PMID: 35536578;

11. Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, Schmitt SK, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clin Infect Dis. 2015 Sep 15;61(6):e26-46. doi: 10.1093/cid/civ482. Epub 2015 Jul 29. PMID: 26229122.

11. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013 Jan;56(1):e1-e25. doi: 10.1093/cid/cis803. Epub 2012 Dec 6. PMID: 23223583.

12. Association of Medical Microbiology and Infectious Disease Canada and Canadian Orthopaedic Association Joint Statement: ORAL TREATMENT FOR BONE AND JOINT (INCLUDING PROSTHETIC JOINT) INFECTIONS. Accessed 6/15/26

13. Duke University Hospital Oral Antibiotic Transition Guidance for Bone and Joint Infections (BJIs) in Adult Patients. Accessed 6/15/26

15. Hawkins MR, Thottacherry E, Juthani P, Aronson J, Chang A, Amanatullah DF, et al. Implementing Oral Antibiotics for Bone and Joint Infections: Lessons Learned and Opportunities for Improvement. Open Forum Infect Dis. 2024 Nov 16;11(12):ofae683. doi: 10.1093/ofid/ofae683. PMID: 39660026

16. Lin L, Li J, Zhang C, Li J, Wu B, Huang Z, et al. Comprehensive analysis of culture-negative periprosthetic joint infection with metagenomics next-generation sequencing. Front Cell Infect Microbiol. 2025 May 9:15:1564488.

16. Goswami K, Clarkson S, Phillips CD, et al. An enhanced understanding of culture-negative periprosthetic joint infection with next-generation sequencing: a multicenter study. J Bone Joint Surg Am. 2022 Sep 7;104(17):1523-29.