PeaceHealth Hospitals
Clinical decision support for Enterobacterales bacteremia from a urinary source.

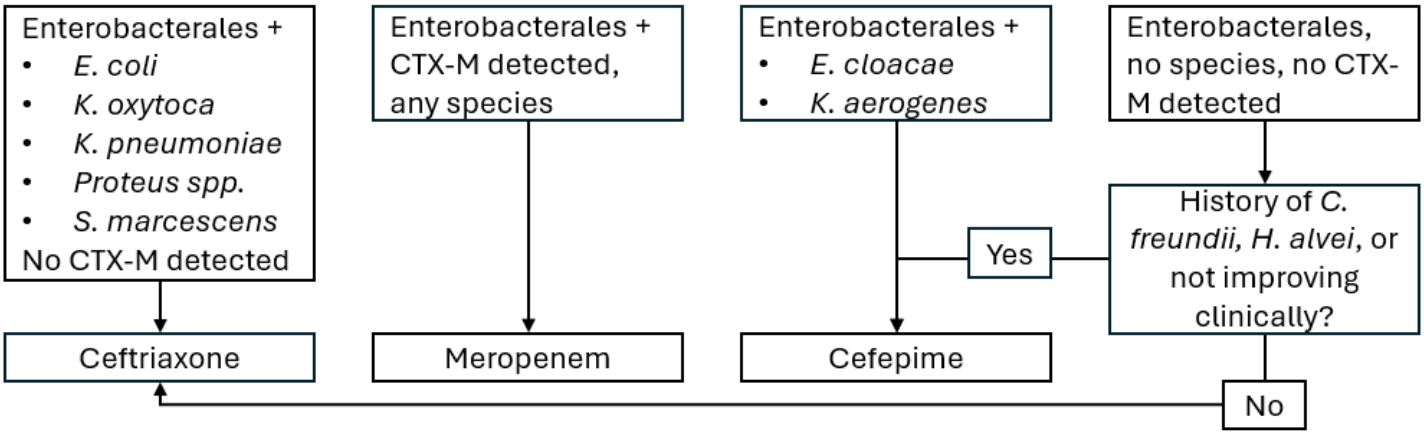
Purpose: Provide treatment algorithms for patients with Enterobacterales bacteremia from urinary source at PeaceHealth hospitals, to encourage evidence-based practice and improve clinical outcomes.

Definitions:
AmpC Producer: *E. cloacae, K. aerogenes, C. freundii,* or *H. alvei* (see separate guideline for details)
Extended spectrum beta-lactamase (ESBL) producer: *E. coli, K. pneumoniae,* miscellaneous non AmpC enterobacterales with non-susceptibility to ceftriaxone (see separate guideline for details)
Fever: 38° C or 100.4° F sustained over 1 hour OR an isolated temperature of 38.3° C or 100.9° F

Inclusion: recommendation for empiric treatment selection or adjustment

- Enterobacterales bacteremia from presumed urinary source, as identified by blood culture DNA identification panel (*Salmonella spp.* bacteremia treatment does not fall under the scope of this guide)
- Patient is hemodynamically stable (e.g. not requiring vasopressor therapy)

Initial treatment recommendations, with species identification but before susceptibility data:



Initial dosing strategies:

Antibiotic	Dose
Ceftriaxone	1g IV Q24 hours
Cefepime	1g IV infused over 3 hours Q8H
Meropenem	1g IV infused over 3 hours Q8H

2 g doses confer no added benefit for susceptible bacteremias and are associated with increased risk of toxicity. Renal dose adjustments and/or loading doses per pharmacy protocol where indicated.

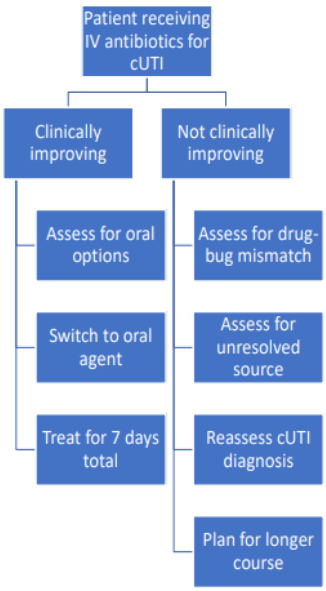
Infectious diseases input recommended for true allergy to 3rd or 4th generation cephalosporins. See PH policy 18669558 for assessment of antibiotic allergy.

Repeat blood cultures are unnecessary in most patients who are improving clinically on antibiotic therapy. Consider repeat blood cultures for those with persistent fevers despite active therapy, concern for endovascular

infection, retained intravascular catheters or other prosthetic devices, and those who have otherwise not clinically improved. Repeat blood cultures should not be obtained until at least 48 hours after initial blood cultures.

Process flow for assessment of response to therapy and definitive treatment:

Figure 1.2: Stepwise assessment of IV to oral switch and duration of antibiotic therapy



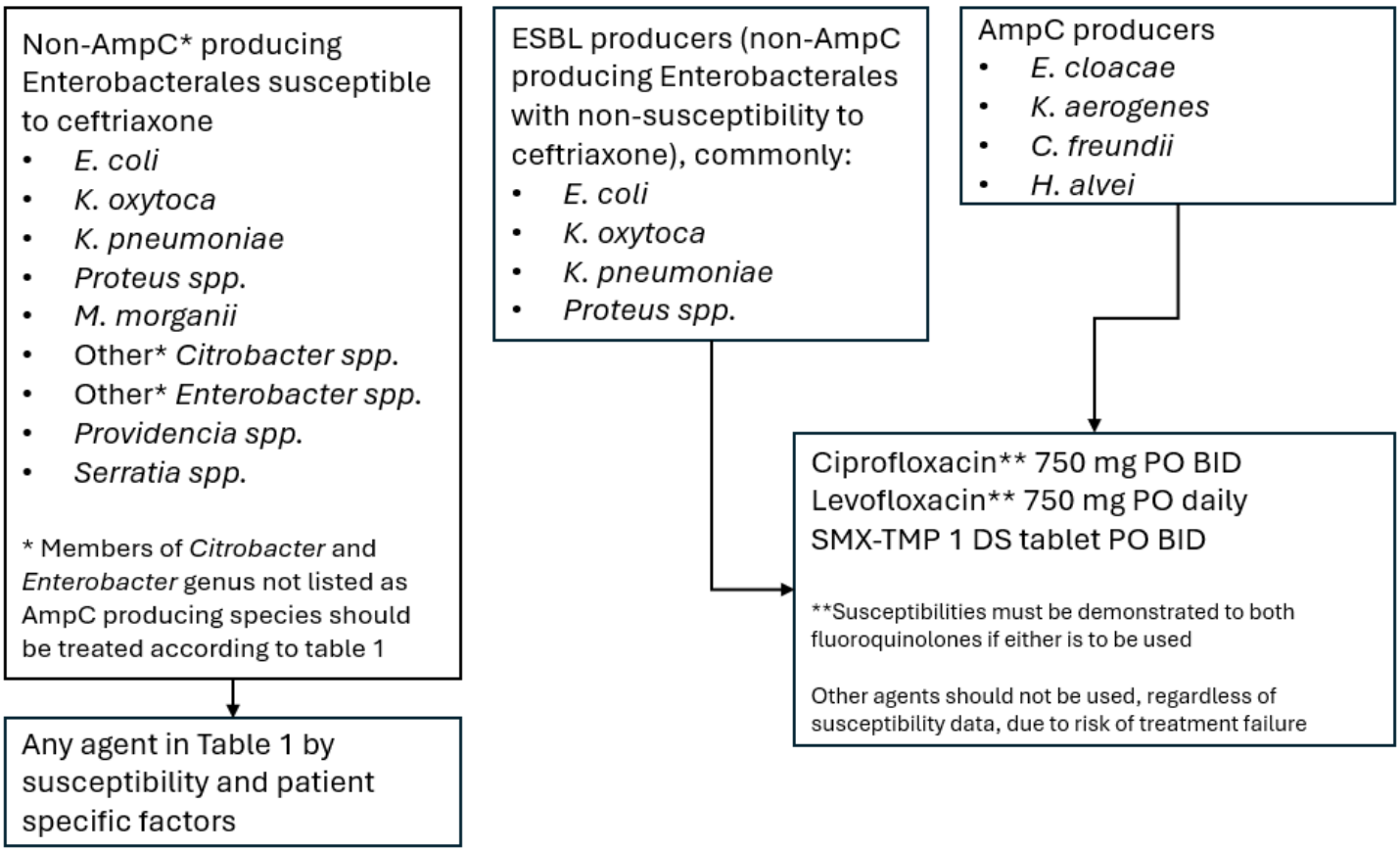
Abbreviations: IV=intravenous, cUTI=complicated UTI. Drug-bug mismatch means that the causative organism is not susceptible to the antibiotic prescribed.

Inclusion: definitive treatment recommendation

- Patient is clinically improving
- No evidence of endovascular infection, osteomyelitis, central nervous system infection, prostatitis, epididymitis, orchitis, perinephric abscess, or retained prosthetic material at the site of infection
- Adequate source control has been achieved
- Culture and susceptibility data are available – patients with no oral options are still candidates for 7-day treatment course with an appropriate IV agent
- For oral (PO) treatment recommendations: patient is able to tolerate PO medications without concern for poor gastrointestinal absorption (see PH policy 17616473 for details)

Definitive treatment recommendations, with culture and susceptibility data:
Fluoroquinolones and SMX-TMP have high oral bioavailability but have less desirable side effect profiles when compared to oral β-lactams. The higher doses or oral beta lactams recommended in Table 1 are expected to reach pharmacokinetic targets. Multiple recent studies demonstrate no significant difference in recurrence of bacteremia or mortality between high-dose β-lactams, SMX-TMP, and oral fluoroquinolones for gram negative bacteremia.

Selection of oral agent for stepdown treatment:



Nitrofurantoin, fosfomycin, or any tetracycline should never be used for bloodstream infections. If no oral options are available, consider infectious diseases input for coordination of IV antibiotics to complete 7 days.

Table 1: Oral agent and dosages for stepdown treatment

Antibiotic	Dose	Notes
Amoxicillin	1 g PO three times daily	Infer from ampicillin susceptibility. 80% bioavailability.
Amoxicillin-clavulanate	875 mg PO twice daily	80% bioavailability
Cephalexin	1000 mg PO three times daily	90% bioavailability
Cefadroxil	1000 mg PO twice daily	90% bioavailability. For outpatient use only if included on partner (KP) formulary

Renal adjustment per pharmacy protocol as indicated

Alternative oral agent and dosages for stepdown treatment

SMX-TMP	800 mg-160 mg (DS) PO twice daily	80% bioavailability. Avoid where alternatives are available in patients with impaired renal function.
Ciprofloxacin	500 mg PO twice daily AmpC or ESBL producers: 750 mg PO twice daily	70% bioavailability. Avoid where alternatives are available in elderly patients, those with cardiac comorbidities, or risk of aortic aneurysm. Susceptibility must be demonstrated to all tested fluoroquinolones prior to use.

Renal adjustment per pharmacy protocol as indicated

Secondary alternative oral agent dosages for stepdown treatment

Cefpodoxime	200 mg PO twice daily	Lower bioavailability (50%) compared with other listed beta lactams
Levofloxacin	750 mg PO once daily	~85% bioavailability. Avoid where alternatives are available in elderly patients, those with cardiac comorbidities, or risk of aortic aneurysm. Susceptibility must be demonstrated to all tested fluoroquinolones prior to use.

Renal adjustment per pharmacy protocol as indicated

Duration of treatment:

7-day treatment duration is recommended for most Enterobacterales bacteremia and is preferred over longer courses. Day 0 is classified as the initiation of active treatment or source control, whichever is later.

Treatment duration of multi-drug-resistant (MDR) pathogens is identical to that of susceptible pathogens, as long as preferred treatment is used.

Special circumstances: consider infectious diseases consultation for total duration of treatment for retained prosthetic material at the site of infection, uncertainty regarding infectious source control, or other unique clinical circumstances.

References:

Trautner BW et al. Complicated urinary tract infections (cUTI): Clinical guidelines for treatment and management. Infectious Diseases Society of America. CID 202. Retrieved 7_2025 from https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/

Tamma PD, Conley AT, Cosgrove SE, et al. Association of 30-day mortality with oral step-down vs continued intravenous therapy in patients hospitalized with enterobacteriaceae bacteremia. JAMA Intern Med. 1 2019;179(3):316-323.10.1001/jamainternmed.2018.6226

Hobbs A et al. Rise of the beta-lactams: a retrospective, comparative cohort of oral beta-lactam antibiotics as stepdown therapy for hospitalized adults with acute pyelonephritis. Antimicrob Stew Health Epdemiol. 2024;4:e102:1-6. 10.1017/ash.2024.70

Saad S, Mina N, Lee C, Afra K. Oral beta-lactam step down in bacteremic E. coli urinary tract infections. BMC Infect Dis. 2020;20(1):785. 10.1186/s12879-020-05498-2

Fosse PE, Brinkman KM, Brink HM, Conner CE, Aden JK, Giancola SE. Comparing outcomes among outpatients treated for pyelonephritis with oral cephalosporins versus first-line agents. Int J Antimicrob Agents. 2022;59(4):106560. 10.1016/j.ijantimicag.2022.106560

Mercuro NJ, Stogsdill P, Wungwattana M. Retrospective analysis comparing oral stepdown therapy for enterobacteriaceae bloodstream infections: fluoroquinolones versus beta lactams. Int J Antimicrob Agents. 2018;51(5):687-692.10.1016/j.ijantimicag.2017.12.007

Nisly SA, McClain DL, Fillius AG, Davis KA. Oral antibiotics for the treatment of Gram negative bloodstream infections: A retrospective comparison of three antibiotic classes. J Glob Antimicrob Resist. 2020;20:74-77. 10.1016/j.jgar.2019.07.026

Alzaidi S, Veillette JJ, May SS, et al. Oral beta-lactams, fluoroquinolones, or trimethoprim-sulfamethoxazole for definitive treatment of uncomplicated Escherichia coli or Klebsiella species bacteremia from a urinary tract source. Open Forum Infect Dis. 2024;11(2):ofad657. 10.1093/ofid/ofad657

McAlister MJ, Rose DT, Hudson FP, Padilla-Tolentino E, Jaso TC. Oral beta-lactams vs fluoroquinolones and trimethoprim/sulfamethoxazole for step-down therapy for Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae bacteremia. Am J Health Syst Pharm. 2023;80(Suppl 1):S33-S41. 10.1093/ajhp/zxac202

Sutton JD, Stevens VW, Chang NN, Khader K, Timbrook TT, Spivak ES. Oral beta lactam antibiotics vs fluoroquinolones or trimethoprim-sulfamethoxazole for definitive treatment of Enterobacterales bacteremia from a urine source. JAMA Netw Open. 2020;3(10):e2020166. 10.1001/jamanetworkopen.2020.20166

Mponponsuo K, Brown KA, Fridman DJ, et al. Highly versus less bioavailable oral antibiotics in the treatment of gram-negative bloodstream infections: a propensity-matched cohort analysis. Clin Microbiol Infect. 2023;29(4):490-497. 10.1016/j.cmi.2022.10.004

Mack T, Hiles JJ, Wrin J, Desai A. Use of fluoroquinolones or sulfamethoxazole trimethoprim compared to beta-lactams for oral step-down therapy in hospitalized patients with uncomplicated Enterobacterales bacteremia. Ann Pharmacother. 2023;57(3):251- 258. 10.1177/10600280221106789

Bjork L, Hopkins T, Yang L, et al. Comparative-effectiveness of oral beta-lactams and fluoroquinolones for stepdown therapy in patients with Enterobacterales bloodstream infections: A retrospective cohort study. Int J Med Sci. 2023;20(4):437-443. 10.7150/ijms.80621

Geyer AC, VanLangen KM, Jameson AP, Dumkow LE. Outcomes of high-dose oral beta-lactam definitive therapy compared to fluoroquinolone or trimethoprim-sulfamethoxazole oral therapy for bacteremia secondary to a urinary tract infection. Antimicrob Steward Healthc Epidemiol. 2023;3(1):e148. 10.1017/ash.2023.435

Casado A, Gimeno A, Aguilar-Guisado M, et al. Safety of early oral ambulatory treatment of adult patients with bloodstream infections discharged from the emergency department. Antimicrob Agents Chemother. 2023;67(11):e0078023. 10.1128/aac.00780-23

Veillette JJ, May SS, Alzaidi S, et al. Real-world effectiveness of intravenous and oral antibiotic stepdown strategies for Gram-negative complicated urinary tract infection with bacteremia. Open Forum Infect Dis. 2024;11(4):ofae193. doi:10.1093/ofid/ofae193

Punjabi C, Tien V, Meng L, Deresinski S, Holubar M. Oral fluoroquinolone or trimethoprim-sulfamethoxazole vs. beta-lactams as step-down therapy for Enterobacteriaceae bacteremia: Systematic review and meta-analysis. Open Forum Infect Dis. 2019;6(10). 10.1093/ofid/ofz364

Kutob LF, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. Effectiveness of oral antibiotics for definitive therapy of Gram-negative bloodstream infections. Int J Antimicrob Agents. 2016;48(5):498-503. 10.1016/j.ijantimicag.2016.07.013

Yahav D, Franceschini E, Koppel F, et al. Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial. *Clin Infect Dis*. 2019;69(7):1091-1098. doi:10.1093/cid/ciy1054

Molina J et al. Seven versus 14 day courses of antibiotics for the treatment of bloodstream infections by Enterobacterales: a randomized, controlled trial. Clin Microbiol Infect. 2022;28(4):550-557. 10.1016/j.cmi.2021.09.001

Keintz M et al. Guidance on management of uncomplicated bloodstream infections from Gram-negative organisms, Retrieved 7_2025 from https://www.unmc.edu/intmed/_documents/id/asp/gram_negative_bacteremia_guidance_8-2023.pdf

UCSF 2025. Gram negative bloodstream infection. Retrieved 7_2025 from:https://idmp.ucsf.edu/content/gram-negative-bloodstream-infection