

Clinical Practice Guideline by Infectious Diseases Society of America (IDSA): 2025 Guideline on Management and Treatment of Complicated Urinary Tract Infections

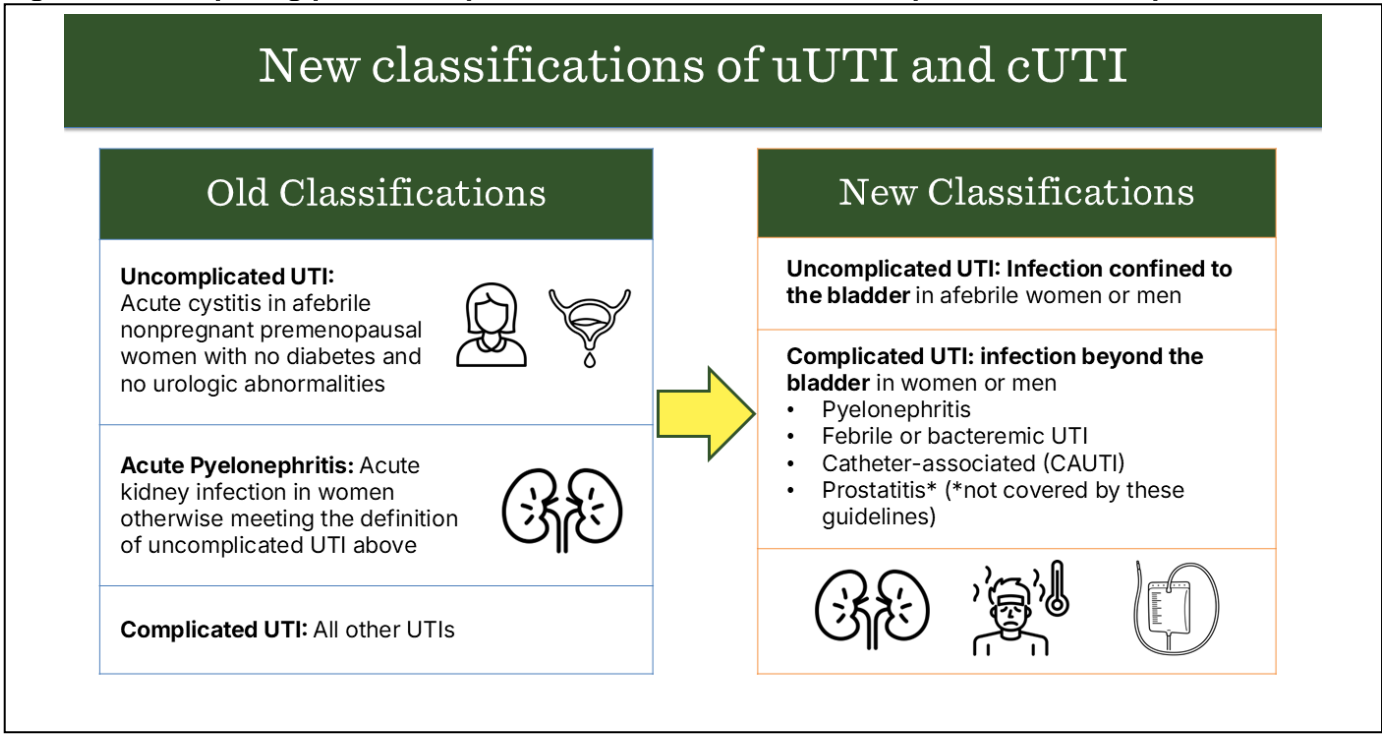
Barbara W. Trautner,¹ Nicolás W. Cortés-Penfield,² Kalpana Gupta,³ Elizabeth B. Hirsch,⁴ Molly Horstman,⁵ Gregory J. Moran,⁶ Richard Colgan,⁷ John C. O'Horo,⁸ Muhammad S. Ashraf,⁹ Shannon Connolly,¹⁰ Dimitri Drekonja,¹¹ Larissa Grigoryan,¹² Angela Huttner,¹³ Gweneth B. Lazenby,¹⁴ Lindsay Nicolle,¹⁵ Anthony Schaeffer,¹⁶ Sigal Yawetz,¹⁷ Valéry Lavergne,^{18,19}

¹ Division of Infectious Diseases, Department of Medicine, Washington University School of Medicine, St. Louis, MO, ²Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, NE, USA, ³Section of Infectious Diseases, Boston VA Health Care System, Boston University School of Medicine, Boston, MA, USA, ⁴Department of Experimental and Clinical Pharmacology, University of Minnesota College of Pharmacy, Minneapolis, MN, USA, ⁵Center for Innovations in Quality, Effectiveness, and Safety, Michael E. DeBakey VA Medical Center, Department of Medicine, Baylor College of Medicine, Houston, TX, USA, ⁶Professor of Clinical Emergency Medicine, David Geffen School of Medicine at UCLA, Olive View-UCLA Medical Center, Los Angeles, CA, USA, ⁷Department of Family and Community Medicine, University of Maryland School of Medicine, Baltimore, MD, USA, ⁸Division of Public Health, Infectious Diseases and Occupational Medicine, Mayo Clinic, Rochester, MN, USA, ⁹Division of Infectious Diseases, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, USA, ¹⁰Associate Medical Director, Planned Parenthood of Orange and San Bernardino Counties, Orange, CA, USA, ¹¹Infectious Disease Section, Minneapolis VA Health Care System, University of Minnesota Medical School, Minneapolis, MN, USA, ¹²Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX, USA, ¹³Division of Infectious Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland, ¹⁴Departments of Obstetrics and Gynecology and Medicine Division of Infectious Diseases, Medical University of South Carolina, Charleston, SC, USA, ¹⁵Faculty of Health Sciences, University of Manitoba School of Medicine, Winnipeg, Manitoba, Canada, ¹⁶Department of Urology, Feinberg School of Medicine Northwestern University, Chicago, IL, USA, ¹⁷Division of Infectious Diseases, Brigham and Women's Hospital, Boston, MA, USA, ¹⁸Division of Medical Microbiology and Infection Control, Department of Pathology & Laboratory Medicine, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada, ¹⁹Department of Clinical Affairs and Practice Guidelines, Infectious Diseases Society of America (IDSA), Arlington, VA, USA

EXECUTIVE SUMMARY

Updated classifications of uncomplicated and complicated urinary tract infections (UTIs)

Figure 1.0 Comparing prior and updated classifications of uncomplicated and complicated UTI



Box 1: Complicated UTI classifications for guidelines purposes (intended to guide treatment not diagnosis)

- Clinical presentation:
 - o Complicated UTI is accompanied by symptoms which suggest an infection extending beyond the bladder, including:
 - Fever
 - Other signs or symptoms of systemic illness (including chills, rigors, or hemodynamic instability)
 - Flank pain
 - Costovertebral angle tenderness
 - o Pyelonephritis is encompassed in complicated UTI.
 - o UTI with systemic symptoms associated with transurethral, suprapubic, or intermittent catheterization is encompassed in complicated UTI.
- Populations:
 - o Patients with complicated UTIs may have an indwelling urinary catheter, neurogenic bladder, urinary obstruction, or urinary retention as an underlying condition.
 - o These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

Box 2: Uncomplicated UTI classifications for guidelines purposes (intended to guide treatment, not diagnosis)

- Clinical presentation:
 - o A clinical syndrome characterized by local bladder signs and symptoms such as dysuria, urgency, frequency, and suprapubic pain.
 - o Uncomplicated UTI is presumed to be confined to the bladder and is defined by absence of signs or symptoms which suggest an infection extending beyond the bladder:
 - No fever, unless explained by a non-UTI cause
 - No other signs or symptoms of systemic illness (including chills, rigors, or unstable vital signs), unless explained by a non-UTI cause
 - No flank pain
 - No costovertebral angle tenderness
- Populations:
 - o Uncomplicated UTI can occur in females or males, patients with underlying urologic abnormalities, patients with immunocompromise, and persons with diabetes. Recurrent UTI can be uncomplicated.
 - o Patients with urinary catheters (including transurethral, suprapubic, and intermittent catheterization), stents, and percutaneous nephrostomy tubes generally do not have uncomplicated UTI.
 - o These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

Selection of Antibiotic Therapy for Complicated UTI

A. Initial Selection among Empiric Antibiotic Options for Complicated UTI

In patients with cUTI, which classes of empiric antibiotic therapy should initially be prioritized?

Recommendations:

- a) For patients with **sepsis** due to complicated UTI, we suggest **initially selecting among** the following antibiotics, using the four-step assessment (**Figure 1.1**): third- or fourth-generation cephalosporins, carbapenems, piperacillin-tazobactam, or fluoroquinolones, rather than newer agents (novel beta lactam-beta lactamase inhibitors, cefiderocol, plazomicin) or older aminoglycosides (*conditional recommendation, very low to moderate certainty of evidence*).

Remarks:

- See **Table 1.1** for a more complete list of empiric antibiotic therapy options.
- Please refer to the four-step approach in **Figure 1.1** to choose among these antibiotics for the specific patient (i.e., severity of illness, risk factors for having resistant uropathogen, patient-specific considerations, and antibiogram).
- Agents with broader spectrum of activity against organisms other than Enterobacterales (e.g. *Pseudomonas aeruginosa*, enterococci, or methicillin-resistant *Staphylococcus aureus*) may be considered for patients with sepsis in whom the diagnosis of cUTI is not clear or who are suspected to have cUTI due to these pathogens.

Comments:

- This recommendation places a higher value on providing early, appropriate empiric antibiotic therapy to prevent mortality while deferring stewardship considerations to definitive therapy.
- The certainty of evidence was moderate for all classes of antibiotics, except for third and fourth generation cephalosporins, and older aminoglycosides, for which the certainty of evidence was very low.

- b) For patients with suspected complicated UTI without sepsis, we suggest **initially selecting among** the following antibiotics, using the four-step assessment (**Figure 1.1**): third- or fourth-generation cephalosporins, piperacillin-tazobactam, or fluoroquinolones, rather than carbapenems and newer agents (novel beta lactam-beta lactamase inhibitors, cefiderocol, plazomicin) or older aminoglycosides (*conditional recommendation, very low to moderate certainty of evidence*).

Remarks:

- See **Table 1.1** for a more complete list of empiric antibiotic therapy options.
- Please refer to the four-step approach in **Figure 1.1** to choose among these antibiotics for the specific patient (i.e., severity of illness, risk factors for having resistant uropathogen, and patient-specific considerations).
- Other agents (e.g., trimethoprim-sulfamethoxazole, amoxicillin-clavulanate, first or second-generation cephalosporins) are less well studied but may be appropriate in select settings or situations for empiric oral treatment of cUTI.

Comments:

- This recommendation places a higher value on antibiotic stewardship considerations in patients with cUTI who are not septic and in whom the risk of infection-related mortality is low while also considering costs, resources, and practical aspects of antibiotic administration
- The certainty of evidence was moderate for all classes of antibiotics, except for third and fourth generation cephalosporins and older aminoglycosides, for which the certainty of evidence was very low.

Table 1.1: Potential Empiric Antibiotics for cUTI[^] prior to using the four-step approach to choose among these options

Four-Step Approach to choose among these antibiotics: Assess (1) severity of illness, (2) risk factors for resistance, (3) patient-specific considerations, and (4) if septic, consider the antibiogram. See discussion below for details of the four steps.

| Condition of the Patient | Preferred | Alternative |
|--------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sepsis with or without shock ^{**} | Third or fourth generation cephalosporins, [*] carbapenems, [#] piperacillin-tazobactam, fluoroquinolones ^{&} | Novel beta lactam-beta lactamase inhibitors, ⁺ ceftiderocol, plazomicin, or older aminoglycosides [%] |
| Without sepsis, IV route of therapy | Third or fourth generation cephalosporins, [*] piperacillin-tazobactam, or fluoroquinolones ^{&} | Carbapenems, [#] newer agents (novel beta lactams-beta lactamase inhibitors, ⁺ ceftiderocol, plazomicin), or older aminoglycosides [%] |
| Without sepsis, oral route of therapy | Fluoroquinolones ^{&} or trimethoprim-sulfamethoxazole | Amoxicillin-clavulanate or oral cephalosporins (see Table 3.1) |

[^]Difficult-to-treat resistant pathogens may require use of drugs not listed here (e.g., colistin); refer to IDSA Antimicrobial Resistance guidance.

^{**}Sepsis is life-threatening organ dysfunction related to infection, identified by SOFA score of 2 or higher. Screening tools such as qSOFA or SIRS may be useful for presumptive identification. In sepsis with shock, in step 4 choose an antibiotic for which the susceptibilities of the most relevant organisms are at least 90%. In sepsis without shock, in step 4 choose an antibiotic for which the susceptibilities of the most relevant organisms are at least 80%.

^{*}Third and fourth generation IV cephalosporins include: ceftriaxone, ceftazidime, cefotaxime, and cefepime. (see **Table 2.1 & 3.1**, Dosing of IV and oral antibiotics for cUTI).

[&]The fluoroquinolones approved for UTI currently include ciprofloxacin and levofloxacin.

[#]The carbapenems currently include imipenem-cilastatin, doripenem, meropenem, and ertapenem.

⁺The novel beta lactam-beta lactamase inhibitors currently include ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-cilastatin-relebactam.

[%]Older aminoglycosides include gentamicin, amikacin, and tobramycin.

This table was created in 2025; new drugs approved after this date may also be appropriate choices.

Please note that nitrofurantoin and oral fosfomycin are generally not appropriate choices for cUTI because they may not achieve adequate levels in renal parenchyma and blood.

B. Process to Guide Empiric Antibiotic Choice for Complicated UTI

To optimize the selection of empiric antibiotic therapy for patients with suspected complicated UTI, we propose the following four-step approach: 1) assess the severity of illness (for initial prioritization of empiric antibiotic therapy), 2) consider patient-specific risk factors for resistant uropathogens (for optimization of coverage), 3) evaluate other patient-specific considerations (to reduce the risk of adverse events), and 4) for patients with sepsis, consult a relevant local antibiogram if available (to further improve the likelihood of giving appropriate empiric therapy in septic patients).

STEP 1: SEVERITY OF ILLNESS (initial prioritization of empiric antibiotic therapy)

In patients with suspected cUTI (including pyelonephritis), should selection of empiric antibiotic therapy be guided by severity of illness?

Recommendation:

- I. For patients with suspected complicated UTI (including pyelonephritis), we suggest that the selection of empiric antibiotic therapy be initially guided by the severity of illness, specifically by whether the patient is in sepsis or not (*conditional recommendation, very low certainty of evidence*).

Remarks:

-Sepsis is defined per the Sepsis-3 Task Force as life-threatening organ dysfunction caused by a dysregulated host response to infection. These patients can be identified by SOFA score increase of 2 points or more, reflecting an in-hospital mortality greater than 10%, or presumptively identified with screening tools such as qSOFA or SIRS.^{20,21}

STEP 2: PATIENT-SPECIFIC RISK FACTORS FOR RESISTANT UROPATHOGENS (optimization of coverage)

In patients with cUTI (including pyelonephritis), should selection of empiric antibiotic therapy be guided by patient-specific prior urine culture results and patient-specific risk factors for resistant uropathogens to optimize selection)?

Recommendations:

- I. In patients with complicated UTI (including acute pyelonephritis), we suggest avoiding antibiotics to which the patient has had a resistant pathogen isolated from the urine previously (*conditional recommendation, very low certainty of evidence*).

Remarks:

-More recent urine cultures may be a better guide than more distant urine cultures.
-The time frame for paired cultures (urine samples collected from the same patient at different occasions) varied, but the median was 3-6 months.

- II. In patients with complicated UTI (including acute pyelonephritis), we suggest avoiding fluoroquinolones if the patient has been exposed to that class of antibiotic in the past 12 months (*conditional recommendation, very low certainty of evidence*).

Remarks: More recent antibiotic exposure may be a better guide than more distant antibiotic exposure.

STEP 3: OTHER PATIENT-SPECIFIC CONSIDERATIONS (prevention of possible undesirable events)

In patients with cUTI (including pyelonephritis), should selection of empiric antibiotic therapy be further guided by patient-specific considerations?

Recommendation:

In patients suspected of cUTI, empiric antibiotic therapy selection should account for patient-specific considerations (e.g. risk of allergic reaction, contraindications, or drug-drug interactions) to avoid preventable adverse events (*good practice statement*).

STEP 4: ANTIBIOGRAM (tailoring empiric antibiotic therapy in septic patients)

In patients with cUTI (including pyelonephritis), should selection of empiric antibiotic therapy be further tailored by consulting an antibiogram?

Recommendations:

- I. In patients with sepsis assumed to be caused by complicated UTI (including acute pyelonephritis), we suggest using an antibiogram to further tailor empiric antibiotic choice **only if** the antibiogram is local, recent, and relevant to the patient (*conditional recommendation, very low certainty of evidence*).

Remarks:

-An antibiogram is considered local if derived from the same healthcare facility, recent if based on data from the prior 12 months and relevant to the patient if based on organisms from a similar patient population.

-If an antibiogram is being used to further tailor empirical antibiotic choice, consider selecting an antibiotic for which 90% or more of the most relevant organism(s) are susceptible in patients in septic shock, or for which 80% or more of the most relevant organism(s) are susceptible in patients with sepsis without shock. These cutoffs are based on modeling of increased mortality risk associated with inappropriate empiric antibiotics in sepsis and septic shock.

-Septic shock is defined by the Sepsis-3 Task Force as a subset of sepsis in which despite volume resuscitation, vasopressors are required to maintain blood pressure and serum lactate level is greater than 2 mmol/L, reflecting an in-hospital mortality greater than 40%.^{20,21}

- II. For patients with suspected complicated UTI without sepsis (including acute pyelonephritis), we make no specific recommendation about using an antibiogram to further tailor empiric antibiotic choice (*no recommendation, knowledge gap*).

Remarks:

-Patients who are not septic have a lower risk of mortality from cUTI (less than or equal to 5%) and initial inappropriate empiric antibiotic choice has little impact on mortality. Routine use of broader-spectrum agents in suspected complicated UTI without sepsis may drive antimicrobial resistance without substantial patient benefit.

Table 2.1: Dosing of intravenous (IV) antibiotics for complicated UTI used in clinical studies presented in alphabetical order

| Drug | Dosing regimen used in clinical trials for patients with normal renal function |
|--------------------------------|--------------------------------------------------------------------------------|
| Cefepime | 1-2g every 8 to 12 hours ^{1,2} |
| Cefepime-enmetazobactam | 2g/0.5g (infused over 2 hours) every 8 hours ³ |
| Cefiderocol | 2g (infused over 3 hours) every 8 hours ^{4,5} |
| Cefotaxime | 1-2g every 8 hours ⁶ |
| Ceftazidime | 1-2g every 8 hours ^{7,8} |
| Ceftazidime-avibactam | 2.5g (infused over 2 hours) every 8 hours ⁹⁻¹¹ |
| Ceftolozane-tazobactam | 1.5g every 8 hours ¹² |
| Ceftriaxone | 1-2g daily ^{13,14} |
| Ertapenem | 1g daily ¹⁴ |
| Fosfomycin | 6g every 8 hours ¹⁵ |
| Imipenem-cilastatin | 500mg every 6 hours ^{11,16} 1g every 8 hours ⁵ |
| Imipenem-cilastatin-relebactam | 500mg/125mg every 6 hours ¹⁶ |
| Meropenem | 1g every 8 hours ^{13,17} |
| Meropenem-vaborbactam | 2g/2g (infused over 3 hours) every 8 hours ¹⁸ |
| Piperacillin-tazobactam | 4.5g every 8 hours ^{3,15,18} |
| Plazomicin | 10-15mg/kg daily ^{17,19} |

Table 2.1 includes IV dosing for cUTI based on review of randomized controlled trials among patients with complicated UTI.

C. Selection of Definitive Antibiotic Therapy for Complicated UTI

In patients with microbiologically confirmed cUTI, should definitive effective antibiotic therapy be targeted based on the results of urine culture rather than continuing empiric broad-spectrum antibiotics?

Recommendation:

- I. In patients with confirmed complicated UTI, we suggest selecting a definitive effective antibiotic with a targeted spectrum based on the results of urine culture (identification and susceptibility) as soon as these are available, rather than continuing empiric broad-spectrum antibiotics for the complete duration of treatment (*conditional recommendation, low certainty of the evidence*).

Comment:

-This recommendation places a high value on de-escalating antibiotic therapy based on culture results (stewardship considerations) while optimizing the effectiveness of therapy (improving clinical cure and reducing recurrence of infection). De-escalation may be less practical in cases of cUTI managed in the outpatient setting.

Timing of Intravenous to Oral Antibiotics Transition for Complicated UTI

In patients who are being treated parenterally for cUTI, are clinically improving, can take an oral medication and for whom an oral option is available, should parenteral therapy be transitioned to oral rather than continued for the complete duration of therapy?

Recommendations

- I. In patients with complicated UTI (including acute pyelonephritis) treated initially with parenteral therapy who are clinically improving, able to take oral medication, and for whom an effective oral option is available, we suggest transitioning to oral antibiotics rather than continuing parenteral therapy for the remaining treatment duration (*conditional recommendation, low certainty of the evidence*)

Comments:

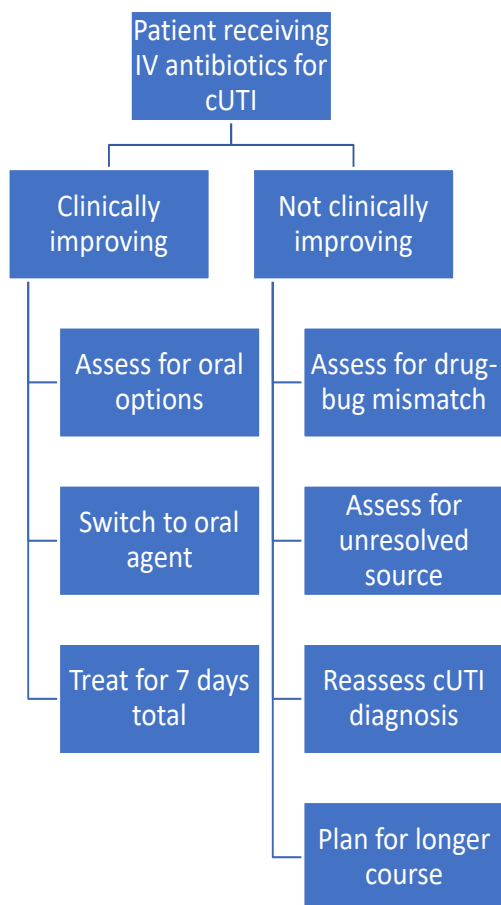
- This recommendation places a high value on reducing avoidable intravenous catheter-related adverse events, costs, and resources, as well as taking into account practical aspects of antibiotic administration.
- The trials supporting this recommendation mostly excluded patients with indwelling urinary catheters, sepsis or septic shock, immunocompromised states, severe renal insufficiency, and functional or structural abnormalities of the urinary tract. Some patients in these subpopulations may need an individualized plan of therapy.
- An effective antimicrobial agent means that the antibiotic achieves therapeutic levels in the urine and relevant tissue and is active against the causative pathogen.
- Refer to **Figure 1.2** for a stepwise assessment of the intravenous to oral switch and the duration of antibiotic therapy.

- II. In patients presenting with complicated UTI (including acute pyelonephritis) and associated Gram-negative bacteremia treated initially with parenteral therapy who are clinically improving, able to take oral medication, and for whom an effective oral option is available, we suggest transitioning to oral antibiotics rather than continuing parenteral therapy for the remaining treatment duration (*conditional recommendation, very low certainty of the evidence*).

Comments:

- The trials supporting this recommendation mostly included patients who were afebrile, hemodynamically stable, and had achieved source control (relief of any urinary obstruction) before transitioning to oral antibiotics.
- An effective antimicrobial agent for bacteremic patients means that the antibiotic achieves therapeutic levels in the bloodstream, urine, and relevant tissue and is active against the causative pathogen.
- Refer to **Figure 1.2** for a stepwise assessment of the intravenous to oral switch and the duration of antibiotic therapy.

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.

Table 1.2: Dosing of oral antibiotics for complicated UTI (in alphabetical order)

| Drugs | Oral absorption (%) | Urinary excretion (%) | Dose for patients with normal renal function |
|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| Amoxicillin-clavulanate | 80 (amoxicillin) ²² variable (clavulanate) ²³ | 50-70 (amoxicillin) ²² 25-40% (clavulanate) ²² | 875mg-125mg every 8 to 12 hours ²⁴⁻³² Other regimens may be more effective ^a |
| Cefixime | 50 ³³ | 50 ³³ | 400mg once daily ³⁴ |
| Cefpodoxime | 50 ³³ | 80 ³³ | 200mg to 400mg every 12 hours ^{31,35,36} |
| Ceftibuten | 75-90 ³³ | 73 ³³ | 9mg/kg daily (children) ^b 400mg daily or 200mg every 12 hours (adults) ^{37,38} |
| Cefuroxime | 52 ^{33,39} | 90 ^{33,39} | 500mg every 12 hours ^{31,40} |
| Cephalexin | 90 ³³ | 90 ³³ | 500mg to 1000mg every 6 hours ^{24-29,32,41,42} Other regimens may be more effective ^a |
| Ciprofloxacin | 70 ⁴³ | 40-50 ⁴³ | 500mg to 750mg every 12 hours ^{28,31,41,44,45} |
| Levofloxacin | 99 ⁴⁶ | 64-100 ⁴⁶ | 500mg to 750mg daily ^{19,36,41,45} |
| Other oral beta-lactams (e.g. amoxicillin, cefadroxil, cefaclor, cefdinir) | Comparative clinical outcomes data vs highly bioavailable oral alternatives are more limited and/or discouraging; consider use with infectious disease pharmacist consultation if alternatives are not available. | | |
| Trimethoprim-sulfamethoxazole | 70-90 ⁴⁷ | 84 (sulfamethoxazole), 66 (trimethoprim) ⁴⁷ | 800mg-160mg every 12 hours ^{31,44} |

Duration of Antibiotics for Complicated UTI

In patients presenting with complicated UTI (cUTI) with a clinical response to therapy, should total duration of antibiotics be prolonged to >7 days rather than shorter (<=7 days)?

Recommendations:

- I. In patients presenting with complicated UTI (including acute pyelonephritis) and who are improving clinically on effective therapy, we suggest treating with a shorter course of antimicrobials, using either 5-7 days of a fluoroquinolone (conditional recommendation, moderate certainty of evidence) or 7 days of a non-fluoroquinolone antibiotic (*conditional recommendation, very low certainty of evidence*), rather than a longer course (10-14 days).

Definitions:

- An effective antimicrobial agent achieves therapeutic levels in the urine and relevant tissue and is active against the causative pathogen.
- The duration of therapy is counted from the first day of effective antibiotic therapy.

Comments:

- Most studies supporting this recommendation excluded patients with indwelling urinary catheters, severe sepsis, immunocompromising conditions, abscesses in the urinary tract, chronic kidney disease, bacterial prostatitis, complete urinary obstruction, or undergoing urologic surgical procedures. Some patients in these subpopulations may be at higher risk for complications or treatment failure and may need an individualized duration of therapy.
- Men with febrile UTI in whom acute bacterial prostatitis is suspected may benefit from a longer treatment duration (i.e., 10-14 days), although evidence to guide the optimal duration in this subgroup is lacking.
- This recommendation is driven by evidence from trials that primarily studied fluoroquinolones during a time when fluoroquinolone resistance was less common. Evidence for short courses of oral beta lactams in cUTI is more limited, and higher doses may be required for efficacy.
- Consider evaluation for an ongoing nidus of infection requiring source control in patients who do not have prompt clinical improvement.
- This recommendation places a high value on antibiotic stewardship considerations as well as reducing the burden of antimicrobial administration from a healthcare perspective and reducing the burden of taking antibiotics from a patient perspective.
- Refer to **Figure 1.3** for a stepwise assessment of the intravenous to oral switch and the duration of antibiotic therapy.

- II. In patients presenting with complicated UTI with associated Gram-negative bacteremia and who are improving clinically on effective therapy, we suggest treating with a shorter course (7 days) of antimicrobial therapy rather than a longer course (14 days) (*conditional recommendation, low certainty in the evidence*).

Definitions:

- An effective antimicrobial agent for bacteremic patients means that the antibiotic achieves therapeutic levels in the bloodstream, urine, and relevant tissue and is active against the causative pathogen.
- The duration of therapy is counted from the first day of effective antibiotic therapy.

Comments:

- Men with febrile, bacteremic UTI in whom acute bacterial prostatitis is suspected may benefit from a longer treatment duration (i.e., 10-14 days), although evidence to guide the optimal duration in this subgroup is lacking.
- Consider evaluation for an ongoing nidus of infection requiring source control in patients who do not have prompt clinical improvement.

- This recommendation places a high value on antibiotic stewardship considerations as well as reducing the burden of antimicrobial administration from a healthcare perspective and reducing the burden of taking antibiotics from a patient perspective.
- Refer to **Figure 1.3** for a stepwise assessment of the intravenous to oral switch and the duration of antibiotic therapy.

References

1. Seo YB, Lee J, Kim YK, et al. Randomized controlled trial of piperacillin-tazobactam, cefepime and ertapenem for the treatment of urinary tract infection caused by extended-spectrum beta-lactamase-producing *Escherichia coli*. *BMC Infect Dis*. Jun 7 2017;17(1):404. doi:10.1186/s12879-017-2502-x
2. Badaro R, Molinar F, Seas C, et al. A multicenter comparative study of cefepime versus broad-spectrum antibacterial therapy in moderate and severe bacterial infections. *Braz J Infect Dis*. Oct 2002;6(5):206-18. doi:10.1590/s1413-86702002000500001
3. Kaye KS, Belley A, Barth P, et al. Effect of Cefepime/Enmetazobactam vs Piperacillin/Tazobactam on Clinical Cure and Microbiological Eradication in Patients With Complicated Urinary Tract Infection or Acute Pyelonephritis: A Randomized Clinical Trial. *JAMA*. Oct 4 2022;328(13):1304-1314. doi:10.1001/jama.2022.17034
4. Bassetti M, Echols R, Matsunaga Y, et al. Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial. *Lancet Infect Dis*. Feb 2021;21(2):226-240. doi:10.1016/s1473-3099(20)30796-9
5. Portsmouth S, van Veenhuizen D, Echols R, et al. Cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infections caused by Gram-negative uropathogens: a phase 2, randomised, double-blind, non-inferiority trial. *Lancet Infect Dis*. Dec 2018;18(12):1319-1328. doi:10.1016/S1473-3099(18)30554-1
6. Edlund C, Ternhag A, Skoog Stahlgren G, et al. The clinical and microbiological efficacy of temocillin versus cefotaxime in adults with febrile urinary tract infection, and its effects on the intestinal microbiota: a randomised multicentre clinical trial in Sweden. *Lancet Infect Dis*. Mar 2022;22(3):390-400. doi:10.1016/S1473-3099(21)00407-2
7. Sharifi R, Geckler R, Childs S. Treatment of urinary tract infections: selecting an appropriate broad-spectrum antibiotic for nosocomial infections. *Am J Med*. Jun 24 1996;100(6A):76S-82S. doi:10.1016/s0002-9343(96)00112-x
8. FDA Package insert for FORTAZ (ceftazidime for injection) 2007. https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/050578s053,050634s020lbl.pdf
9. Carmeli Y, Armstrong J, Laud PJ, et al. Ceftazidime-avibactam or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* complicated urinary tract infections or complicated intra-abdominal infections (REPRISE): a randomised, pathogen-directed, phase 3 study. *Lancet Infect Dis*. Jun 2016;16(6):661-673. doi:10.1016/S1473-3099(16)30004-4
10. Wagenlehner FM, Sobel JD, Newell P, et al. Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program. *Clin Infect Dis*. Sep 15 2016;63(6):754-762. doi:10.1093/cid/ciw378
11. Vazquez JA, Gonzalez Patzan LD, Stricklin D, et al. Efficacy and safety of ceftazidime-avibactam versus imipenem-cilastatin in the treatment of complicated urinary tract infections, including acute pyelonephritis, in hospitalized adults: results of a prospective, investigator-blinded, randomized study. *Curr Med Res Opin*. Dec 2012;28(12):1921-31. doi:10.1185/03007995.2012.748653
12. Wagenlehner FM, Umeh O, Steenbergen J, Yuan G, Darouiche RO. Ceftolozane-tazobactam compared with levofloxacin in the treatment of complicated urinary-tract infections, including pyelonephritis: a randomised, double-blind, phase 3 trial (ASPECT-cUTI). *Lancet*. May 16 2015;385(9981):1949-56. doi:10.1016/S0140-6736(14)62220-0
13. Sojo-Dorado J, Lopez-Hernandez I, Rosso-Fernandez C, et al. Effectiveness of Fosfomycin for the Treatment of Multidrug-Resistant *Escherichia coli* Bacteremic Urinary Tract Infections: A Randomized Clinical Trial. *JAMA Netw Open*. Jan 4 2022;5(1):e2137277. doi:10.1001/jamanetworkopen.2021.37277
14. Park DW, Peck KR, Chung MH, et al. Comparison of ertapenem and ceftriaxone therapy for acute pyelonephritis and other complicated urinary tract infections in Korean adults: a randomized, double-blind, multicenter trial. *J Korean Med Sci*. May 2012;27(5):476-83. doi:10.3346/jkms.2012.27.5.476
15. Kaye KS, Rice LB, Dane AL, et al. Fosfomycin for Injection (ZTI-01) Versus Piperacillin-tazobactam for the Treatment of Complicated Urinary Tract Infection Including Acute Pyelonephritis: ZEUS, A Phase 2/3 Randomized Trial. *Clin Infect Dis*. Nov 27 2019;69(12):2045-2056. doi:10.1093/cid/ciz181

16. Sims M, Mariyanovski V, McLeroth P, et al. Prospective, randomized, double-blind, Phase 2 dose-ranging study comparing efficacy and safety of imipenem/cilastatin plus relebactam with imipenem/cilastatin alone in patients with complicated urinary tract infections. *J Antimicrob Chemother.* Sep 1 2017;72(9):2616-2626. doi:10.1093/jac/dkx139
17. Wagenlehner FME, Cloutier DJ, Komirenko AS, et al. Once-Daily Plazomicin for Complicated Urinary Tract Infections. *N Engl J Med.* Feb 21 2019;380(8):729-740. doi:10.1056/NEJMoa1801467
18. Kaye KS, Bhowmick T, Metallidis S, et al. Effect of Meropenem-Vaborbactam vs Piperacillin-Tazobactam on Clinical Cure or Improvement and Microbial Eradication in Complicated Urinary Tract Infection: The TANGO I Randomized Clinical Trial. *JAMA.* Feb 27 2018;319(8):788-799. doi:10.1001/jama.2018.0438
19. Connolly LE, Riddle V, Cebrik D, Armstrong ES, Miller LG. A Multicenter, Randomized, Double-Blind, Phase 2 Study of the Efficacy and Safety of Plazomicin Compared with Levofloxacin in the Treatment of Complicated Urinary Tract Infection and Acute Pyelonephritis. *Antimicrob Agents Chemother.* Apr 2018;62(4):doi:10.1128/AAC.01989-17
20. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* Feb 23 2016;315(8):801-10. doi:10.1001/jama.2016.0287
21. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med.* Nov 1 2021;49(11):e1063-e1143. doi:10.1097/CCM.0000000000005337
22. AUGMENTIN (amoxicillin/clavulanate potassium) FDA package insert. 2013. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/050564s053s055,050575s040s042,050597s047s049,050720s026s028,050725s028s030,050726s022s024lbl.pdf
23. De Velde F, De Winter BCM, Koch BCP, Van Gelder T, Mouton JW, consortium C-N. Highly variable absorption of clavulanic acid during the day: a population pharmacokinetic analysis. *J Antimicrob Chemother.* Feb 1 2018;73(2):469-476. doi:10.1093/jac/dkx376
24. 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.* Apr 2024;11(4):ofae193. doi:10.1093/ofid/ofae193
25. 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.* Feb 2024;11(2):ofad657. doi:10.1093/ofid/ofad657
26. 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.* Apr 2023;29(4):490-497. doi:10.1016/j.cmi.2022.10.004
27. 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.* Nov 2016;48(5):498-503. doi:10.1016/j.ijantimicag.2016.07.013
28. 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.* Feb 21 2023;80(Suppl 1):S33-S41. doi:10.1093/ajhp/zxac202
29. 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.* Mar 2020;20:74-77. doi:10.1016/j.jgar.2019.07.026
30. Mercuro NJ, Stogsdill P, Wungwattana M. Retrospective analysis comparing oral stepdown therapy for enterobacteriaceae bloodstream infections: fluoroquinolones versus beta-lactams. *Int J Antimicrob Agents.* May 2018;51(5):687-692. doi:10.1016/j.ijantimicag.2017.12.007
31. 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.* Oct 1 2020;3(10):e2020166. doi:10.1001/jamanetworkopen.2020.20166
32. 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.* Mar 2023;57(3):251-258. doi:10.1177/10600280221106789

33. Marshall WF, Blair JE. The cephalosporins. *Mayo Clin Proc.* Feb 1999;74(2):187-95. doi:10.4065/74.2.187
34. Sanchez M, Collvinent B, Miro O, et al. Short-term effectiveness of ceftriaxone single dose in the initial treatment of acute uncomplicated pyelonephritis in women. A randomised controlled trial. *Emerg Med J.* Jan 2002;19(1):19-22. doi:10.1136/emj.19.1.19
35. 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. doi:10.7150/ijms.80621
36. 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.* Apr 2022;59(4):106560. doi:10.1016/j.ijantimicag.2022.106560
37. Marild S, Jodal U, Sandberg T. Ceftibuten versus trimethoprim-sulfamethoxazole for oral treatment of febrile urinary tract infection in children. *Pediatr Nephrol.* Mar 2009;24(3):521-6. doi:10.1007/s00467-008-0996-6
38. Cronberg S, Banke S, Bergman B, et al. Fewer bacterial relapses after oral treatment with norfloxacin than with ceftibuten in acute pyelonephritis initially treated with intravenous cefuroxime. *Scand J Infect Dis.* 2001;33(5):339-43. doi:10.1080/003655401750173922
39. CEFTIN (cefuroxime axetil) FDA package insert. 2015. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/050605s048,050672s034lbl.pdf
40. Lin K, Zahlanie Y, Ortwine JK, Wei W, Mang NS, Prokesch BC. A retrospective review of oral cephalosporins versus fluoroquinolones for the treatment of pyelonephritis. *PLoS One.* 2022;17(9):e0274194. doi:10.1371/journal.pone.0274194
41. 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. doi:10.1017/ash.2023.435
42. Saad S, Mina N, Lee C, Afra K. Oral beta-lactam step down in bacteremic E. coli urinary tract infections. *BMC Infect Dis.* Oct 21 2020;20(1):785. doi:10.1186/s12879-020-05498-2
43. CIPRO (ciprofloxacin hydrochloride) FDA package insert. 2016. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/050605s048,050672s034lbl.pdf
44. Talan DA, Stamm WE, Hooton TM, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women: a randomized trial. *JAMA.* Mar 22-29 2000;283(12):1583-90. doi:10.1001/jama.283.12.1583
45. Peterson J, Kaul S, Khashab M, Fisher AC, Kahn JB. A double-blind, randomized comparison of levofloxacin 750 mg once-daily for five days with ciprofloxacin 400/500 mg twice-daily for 10 days for the treatment of complicated urinary tract infections and acute pyelonephritis. *Urology.* Jan 2008;71(1):17-22. doi:10.1016/j.urology.2007.09.002
46. Croom KF, Goa KL. Levofloxacin: a review of its use in the treatment of bacterial infections in the United States. *Drugs.* 2003;63(24):2769-802. doi:10.2165/00003495-200363240-00008
47. BACTRIM (sulfamethoxazole and trimethoprim double strength tablets) FDA package insert. 2013. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/017377s068s073lbl.pdf