

Guidelines for Treatment of Urinary Tract Infections





Overview

This document details the Michigan Hospital Medicine Safety (HMS) Consortium preferred antibiotic choices for treatment of uncomplicated and complicated lower urinary tract infections, pyelonephritis, and urinary tract infections with bacteremia. The treatment recommendations highlighted in this document are not meant to be a comprehensive guideline.

This guideline also addresses the appropriate management of asymptomatic bacteriuria which accounts for a substantial burden of unnecessary antimicrobial use.



Intended Use

- The recommendations within this guideline are intended to address the management of positive urine cultures in non-pregnant and non-ICU patients.
- This guideline is not intended for patients undergoing urologic procedures during their hospitalization, patients who have undergone urinary diversion surgery, or have urinary stents or percutaneous nephrostomy tubes.
- Hospitals choice of preferred antibiotics among options provided should also be based on antimicrobial stewardship/infectious diseases recommendations, hospital formulary restrictions, and hospital antibiograms (especially urine antibiograms when available).



Asymptomatic Bacteriuria

National guidelines recommend against testing for asymptomatic bacteriuria, except in select circumstances

 In the **absence of signs or symptoms** (see below) attributable to a urinary tract infection, patients with a positive urine culture and/or pyuria **should not be treated** with antibiotics irrespective of high bacterial colony count, or a multi-drug resistant organism.

 <p>Urine Culture</p> <p>Do NOT Send Urine Culture if none of these symptoms are present or there is an alternative cause for the symptom</p>	Signs & Symptoms
	Fever >38° C or rigors without alternative cause
	Urgency, frequency, dysuria
	Suprapubic pain or tenderness
	Costovertebral pain or tenderness
	New onset mental status changes with leukocytosis (>10,000 cells/mm ³), hypotension (<90 mmHg Systolic) or >= 2 SIRS criteria ¹
	Acute hematuria
	Spasticity or autonomic dysreflexia in patients with spinal cord injury

Exceptions to this recommendation include pregnant patients and patients with asymptomatic bacteriuria prior to a urologic procedure.



Empiric Treatment Recommendations for Lower Urinary Tract Infections, Pyelonephritis, and Urinary Tract Infections with Bacteremia

- **Empiric antibiotic choice** should take into consideration recent previous culture results, prior antibiotic use, antibiotic allergies, and severity of presenting illness.
- **Final antibiotic choice** should be based on antibiotic susceptibilities of the pathogen and take into consideration antibiotic allergies of the patient.
- Recommended duration of treatment is for an effective antibiotic based on culture results.

DEFINITIONS			
Uncomplicated Lower Urinary Tract Infection or Cystitis*			
Female patients without catheters and without any of the co-morbid conditions listed under complicated lower urinary tract infections			
Complicated Lower Urinary Tract Infection or Cystitis*			
<p>Patients with catheter associated-urinary tract infections (CA-UTI) and non-CAUTI associated urinary tract infection in the following categories:</p> <ul style="list-style-type: none"> • Men • Women with the following co-morbid conditions: <table style="width: 100%; border: none;"> <tr> <td style="vertical-align: top; width: 33%;"> <ul style="list-style-type: none"> • nephrolithiasis • urologic surgery • urinary obstruction • urinary retention • spinal cord injury • asplenia • receiving chemotherapy for a malignancy or malignancy not in remission </td> <td style="vertical-align: top; width: 33%;"> <ul style="list-style-type: none"> • moderate/severe liver disease • hemiplegia • congestive heart failure • cardiomyopathy • moderate/severe chronic kidney disease or on hemodialysis • structural lung disease (moderate-severe COPD, bronchiectasis, home oxygen) </td> <td style="vertical-align: top; width: 33%;"> <ul style="list-style-type: none"> • sickle cell disease • chronic anti-coagulation • bedridden or using wheelchair • diabetes mellitus with Hgb A1C >8 % • immunodeficiency or immunosuppressive treatments </td> </tr> </table> 	<ul style="list-style-type: none"> • nephrolithiasis • urologic surgery • urinary obstruction • urinary retention • spinal cord injury • asplenia • receiving chemotherapy for a malignancy or malignancy not in remission 	<ul style="list-style-type: none"> • moderate/severe liver disease • hemiplegia • congestive heart failure • cardiomyopathy • moderate/severe chronic kidney disease or on hemodialysis • structural lung disease (moderate-severe COPD, bronchiectasis, home oxygen) 	<ul style="list-style-type: none"> • sickle cell disease • chronic anti-coagulation • bedridden or using wheelchair • diabetes mellitus with Hgb A1C >8 % • immunodeficiency or immunosuppressive treatments
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Uncomplicated Pyelonephritis			
Female patients with pyelonephritis without catheters or any of the co-morbid conditions listed in the definition for complicated lower UTI			
Complicated Pyelonephritis			
Patients with pyelonephritis not meeting the definition for uncomplicated pyelonephritis			

*Excluding patients with pyelonephritis, bacteremia, or sepsis

Uncomplicated Lower Urinary Tract Infection or Cystitis

Antibiotic	Duration	Considerations
Nitrofurantoin ²	5 days	Avoid in CrCl < 30ml/min
Fosfomycin ³	1 dose	<ul style="list-style-type: none"> •Cost ~\$60 / dose •May not be available at some retail pharmacies
Trimethoprim-sulfamethoxazole	3 days	Increasing <i>E. Coli</i> resistance
Alternative		
IV beta-lactam ⁶ or Oral beta-lactam ⁴	3-7 days	

Fluoroquinolones should be reserved for uncomplicated cystitis when other oral antibiotic options are not feasible because of their propensity for collateral damage (antibiotic resistance, *C.difficile* infection, and other adverse effects⁵). When a fluoroquinolone is used, the duration of treatment is 3 days.

Complicated Lower Urinary Tract Infections or Cystitis

Antibiotic	Duration*	Considerations
Nitrofurantoin ²	7 days	Avoid in CrCl < 30ml/min
Fosfomycin ³	Q 48 hrs X 3-5 doses	<ul style="list-style-type: none"> •Cost ~\$60 / dose •May not be available at some retail pharmacies
Trimethoprim-sulfamethoxazole	7 days	Increasing <i>E. Coli</i> resistance
Oral beta-lactam ⁴ , IV beta-lactam ⁶ , or Aztreonam in setting of severe PCN or Cephalosporin allergy	7 days	

*Total antibiotic duration of 7 days (oral, IV, or combination) is usually appropriate, but delayed response to therapy may warrant 10-14 days of therapy. A single dose of Fosfomycin or a 3-day treatment course for other antibiotics can be used for women ≤ 65 years who develop a CA-UTI without upper urinary tract symptoms after the indwelling catheter has been removed.

Fluoroquinolones should be reserved for complicated lower UTI when other oral antibiotic options are not feasible because of their propensity for collateral damage (antibiotic resistance, *C.difficile* infection, and other adverse effects⁵). When a fluoroquinolone is used, the duration of treatment is 5-7 days unless there is a delayed response to therapy.

Uncomplicated Pyelonephritis	
Antibiotic	Duration
Trimethoprim-sulfamethoxazole	7-14 days
Fluoroquinolones	5-7 days
Beta-lactams	IV beta-lactam therapy ⁶ : 7 days IV beta-lactam therapy ⁶ followed by oral beta-lactam ⁴ or oral trimethoprim-sulfamethoxazole therapy: 7-14 days
Complicated Pyelonephritis and UTI with Bacteremia	
Complicated Pyelonephritis: 7-14 days	
UTI with Bacteremia: 7-14 days <i>Shorter courses of therapy (7-days) with a fluoroquinolone or IV beta-lactam can be considered in female patients without co-morbid conditions who are bacteremic secondary to pyelonephritis or cystitis/lower UTI who have rapid clinical response to therapy</i>	

- Nitrofurantoin and Fosfomycin should not be used for pyelonephritis, upper urinary tract infection, or patients with bacteremia.
- Due to potential complications from PICC lines (e.g. DVT, CLABSI), oral fluoroquinolones are preferred over PICC line placement for IV antibiotics when the urinary pathogen is susceptible and there are no contraindications to fluoroquinolones.
- Oral beta-lactams are associated with lower efficacy and higher relapse rates compared to trimethoprim-sulfamethoxazole and fluoroquinolones. If a beta-lactam is used then initial therapy should be IV therapy followed by oral beta-lactam (assuming uropathogen is susceptible).
- A shorter course of therapy (<14 days) is not appropriate for *Staphylococcus Aureus* bacteremia and another source of infection (outside of the genitourinary tract) should be considered.



Appendix

Antibiotic	Dose**
Trimethoprim-sulfamethoxazole (160 mg/800 mg)*	1 DS tablet po BID
Nitrofurantoin**	100 mg po BID
Fosfomycin	3 g dose (see tables for complicated and uncomplicated lower UTI)
Amoxicillin-clavulanate*	875mg po BID Uncomplicated Cystitis: 500 mg po BID
Cephalexin*	500 mg po BID-QID Uncomplicated Cystitis: 500 mg po BID
Cefpodoxime*	100-200 mg po BID Uncomplicated Cystitis: 100 mg po BID
Cefdinir*	300 mg po BID
Cefazolin*	1-2g IV q 8 hr
Cefuroxime*	500 mg po BID 750 mg-1.5g IV q 8 hr Uncomplicated Cystitis: 250 mg po BID
Piperacillin-tazobactam*	3.375 g IV q 6 hr or 4.5 g IV q 6-8 hr
Ceftriaxone	1-2 g IV once daily
Cefepime*	1-2 g IV q 8-12 hr
Aztreonam*	1-2 g IV q 8 hr
Ertapenem*	1 gm IV QD
Meropenem	500 mg IV q6 hr or 1g IV q 8 hr
Levofloxacin*	250-750 mg QD Uncomplicated Cystitis: 250 mg po QD Uncomplicated Pyelonephritis: 7-day duration: 500 mg po QD 5-day duration: 750 mg po QD
Ciprofloxacin*	250-750 mg po BID 400 mg IV q12 hr Uncomplicated Cystitis: 250 mg po BID Uncomplicated Pyelonephritis: 500 mg po BID

* Dose adjustment needed based on renal function

**Dose depends on disease state (Uncomplicated UTI, Complicated UTI, Pyelonephritis), severity of presentation (e.g. septic shock, severe sepsis), presence of bacteremia, and susceptibilities of the pathogen



Footnotes

1. SIRS Criteria: Heart rate greater than 90bpm, respiratory rate greater than 20 breaths per minute or PaCO₂ <32mmHg, temperature less than 36° C, temperature greater than 38° C, white blood count (less than 4,000 cells/mm³, greater than 12,000 cells/ mm³, or greater than >10% immature [band] forms).
2. The Beers Criteria recommends avoiding use in geriatric patients >65 with a CrCl< 30 mL/min. (American Geriatric Society 2015, Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015).
3. Fosfomycin susceptibilities may not be routinely available as part of standard antimicrobial susceptibility testing. Fosfomycin susceptibilities have only been established for *E.coli* and *Enterococcus* species by the Clinical and Laboratory Standards Institute, but there is data and clinical experience supporting use of the same susceptibility breakpoints for other members of the *Enterobacteriaceae* group.
4. Examples of oral beta-lactams include, but are not limited to Amoxicillin-Clavulanate, Cephalexin, Cefdinir, Cefuroxime, and Cefpodoxime.
5. In the Unites States, there are high rates of fluoroquinolone resistance among outpatient and inpatient urinary *E.coli* isolates. IDSA guidelines advise against empiric use of fluoroquinolones when *E.coli* resistance exceeds 20%. Other notable adverse effects of fluoroquinolones include - QT interval prolongation and arrhythmia, peripheral neuropathy, tendinopathy, and tendon rupture. In 2016, the FDA placed a black box warning to limit fluoroquinolone use in uncomplicated UTIs due to potential side effects.
6. Examples of IV beta-lactams include but are not limited to Cefazolin, Ceftriaxone, Cefuroxime, Piperacillin-Tazobactam, Cefepime.



Key References

1. Hooton TM, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 international clinical practice guidelines from the Infectious Diseases Society of America. *Clin Infect Dis* 2010;60:625-663.
2. Nicollle L, et al. Infectious Diseases Society of America Guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005; 40:643-54.
3. Gupta K. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103-120.
4. Fox Miriam T, et al. A seven-day course of TMP-SMX may be as effective as a seven-day course of ciprofloxacin for the treatment of pyelonephritis. *Am J of Medicine* 2017;130: 842-845.
5. Moustafa F, et al. Evaluation of the efficacy and tolerance of a short 7 day third generation cephalosporin treatment in the management of acute pyelonephritis in young women in the emergency department. *J Antimicrob Chemother* 2016;71:1660-1664.
6. Eliakim-Raz N, et al. Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection – 7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother* 2013;68:2183-91.
7. Chotiprasitsakul D, et al. Comparing the outcomes of adults with enterobacteriaceae bacteremia receiving short-course versus prolonged-course antibiotic therapy in a multicenter, propensity score-matched cohort. *Clin Infect Dis* 2018;66:172-177.
8. Johnson JR, et al. Acute Pyelonephritis in Adults. *N Engl J Med* 2018;378:48-59.

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