



Adult Urinary Tract Infection (Outpatient) Care Pathway

This Care Pathway is intended to provide guidance for Penn State Health and affiliated providers in the evaluation and treatment of Urinary Tract Infection in adult patients. The guidance provided in this document is based on evidence-based standards. This document provides an approach applicable for most patients; however, providers should use clinical judgement and adapt to individual patients and situations.

BACKGROUND

Urinary tract infections (UTI) are the second most common type of infection in the body, accounting for about 8.1 million visits to health care providers each year.⁽¹⁾ Women are especially prone with a lifetime risk of having a UTI greater than 50 percent. UTIs in men are not as common as in women but can be serious when they occur. A defined care pathway to share with primary care practices, skilled nursing facilities and home health care agencies supports appropriate and timely care for the patients.

QUICK REFERENCE

Clinical Pathway	2
Antibiotic Dosage	3-5
References	6

GOALS

The goals for this care pathway for Urinary Tract Infection are:

1. Improve the accuracy of clinical diagnosis of UTIs.
2. Improve outpatient clinic efficiency in caring for patients with UTIs.
3. Reduce inappropriate prescribing of antibiotics for asymptomatic bacteriuria.
4. Optimize antibiotic therapy for treatment of UTI while minimizing short and long term risks of antibiotic use.
5. Optimize testing and use of laboratory services for UTI.
6. Reduce Emergency Department Visits and Hospital Admissions related to bacteremia and UTI.

OUTCOMES MEASUREMENT

In order to reach our goals for Urinary Tract Infection, Penn State Health Care Partners will measure

1. Appropriate lab assessment in suspected UTI.
2. Appropriate antibiotic selection for uncomplicated UTI, and avoidance of antibiotics for asymptomatic bacteriuria or pyuria.
3. Patients with multiple Emergency Department visits and/or Hospital Admissions related to UTI and bacteremia.

CARE TEAM OPPORTUNITIES

Care Manager: Connect with patients who were hospitalized from a skilled nursing facility for a UTI to confirm and/or coordinate post-infection follow-up care

Pharmacist: Offer provider education for appropriate antibiotic stewardship

Recommendations: The following recommendations are based on the goals and measures listed above as well as general operational practices.

1. Providers/care teams to review their list of patients who have multiple Emergency Department visits and/or Hospital Admissions related to UTI and bacteremia in order to determine adjustments to treatment plan and/or addition of care management services.
2. Practices implement process, to assess, diagnose, and treat patients with potential UTI
3. Providers/Care teams have processes in place to eliminate treatment for asymptomatic bacteriuria (unless indicated for patients with pregnancy or urologic procedures)
4. Practices to develop workflows to address culture results with a resistant organism or drug-bug mismatch.
5. Practices use standard EMR tools for patient education and follow-up.
6. Health systems work to make local service area’s antibiograms available to providers as electronic resources.

(1) Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2006. National health statistics reports; no 8. Hyattsville, MD: National Center for Health Statistics; 2008



Definitions:
Cystitis: Inflammation of the urinary bladder often caused by infection
Pyelonephritis: Inflammation of the kidney as a result of infection
Underlying anatomical conditions: Bladder outlet obstruction, vesico-ureteral reflux, duplicated collecting system or other defects⁽²⁾

(2) Hickling DR, Sun TT, Wu XR. Anatomy and Physiology of the Urinary Tract: Relation to Host Defense and Microbial Infection. *Microbiol Spectr.* 2015;3(4):10.1128/microbiolspec.UTI-0016-2012. doi:10.1128/microbiolspec.UTI-0016-2012

Suspected UTI with local or systemic symptoms?

no → No treatment is needed for asymptomatic bacteriuria, except:
 • Pregnant women
 • About to undergo invasive urologic procedure
 • Some kidney transplant patients

yes → Do symptoms suggest infection is confined to the bladder? (i.e. limited to dysuria, frequency, urgency, suprapubic tenderness)
 (see * below for indication for hospitalization)

Simple Cystitis

Not Simple Cystitis (e.g., Pyelonephritis)

Underlying anatomical conditions?

Symptoms can include flank pain, costovertebral angle (CVA) tenderness, nausea/vomiting, T>38°C, new onset/worsening incontinence, lethargy, or change in mental status.

No → Nitrofurantoin: 5 days
 Trimethoprim/sulfamethoxazole: 3 days (avoid if resistance prevalence is > 20% or if used in previous 3 months)
 Fosfomycin: single dose
 Amoxicillin/clavulanic acid, cefdinir, or cefpodoxime: 3 days (perhaps up to 7 days)
 If required due to inability to take one of the above options (e.g., true allergy, history of resistance, or current resistance):
 Ciprofloxacin or levofloxacin: 3 days (see warning box below)

Yes → Trimethoprim/sulfamethoxazole: 7 days
 Cephalosporins or amoxicillin/clavulanic acid: 7-10 days
 Ciprofloxacin or levofloxacin : 5 days (see warning box below)

Duration of therapy in catheter associated urinary tract infection (CA-UTI):
 • 7 days in patients with prompt resolution of symptoms
 • 10-14 days in patients with delayed response
 • 5-day regimen with levofloxacin may be considered for non-severely ill patients
 • 3-day regimen may be considered in women ≤65 years old with CA-UTI without upper urinary tract symptoms after an indwelling catheter has been removed

Ciprofloxacin and levofloxacin now carry a black box warning that these drugs should NOT be a first choice for simple cystitis.

*Consider hospitalization for parenteral antibiotics for the following:
 -Signs of critical illness or sepsis
 -Persistently high fever or pain
 -Inability to maintain oral hydration or take oral antibiotics
 -Urinary tract obstruction
 -Pyelonephritis in a renal transplant recipient
 Empiric parenteral antibiotic options include: ceftriaxone, cefepime, piperacillin-tazobactam, ertapenem/meropenem (if history of ESBL), ceftolozane-tazobactam (if appropriate), or ceftazidime-avibactam (if history of carbapenem-resistant organism)

Concerns with use of a fluoroquinolone (FQ)? [e.g., at risk for adverse effects or resistant organism]

no → Is local Fluoroquinolone (FQ) resistance >10%?

no → Ciprofloxacin or levofloxacin x 5-7 days
 Follow up on susceptibilities to ensure adequate coverage

yes → Single dose of long-acting parenteral agent:
 -Ceftriaxone (IV or IM)
 -Gentamicin or tobramycin (IV or IM)
 -History of extended spectrum beta-lactamase (ESBL) or other multi-drug resistant (MDR) non-Pseudomonas Gram-negative: ertapenem (IV or IM)
 Followed by:
 -Ciprofloxacin/levofloxacin x 5-7 days OR a non-FQ option listed to the right, depending on prior antibiotic use and personal history of resistance.
 Follow up on susceptibilities to ensure adequate coverage.

yes → Select agent based on prior susceptibilities, avoiding antibiotics used in the past 3 months:
 - Trimethoprim/sulfamethoxazole x 7-10 days
 - Amoxicillin/clavulanic acid x 10-14 days
 - If known to be susceptible: cefadroxil, cephalixin, cefdinir, or cefpodoxime x 10-14 days
 If history of resistance or recent exposure to the above antibiotics, consider an initial dose of a long-acting parenteral agent, followed by PO choice above:
 - Ceftriaxone (IV or IM)
 - Gentamicin or tobramycin (IV or IM)
 - History of extended spectrum beta-lactamase (ESBL) or other multi-drug resistant (MDR) non-Pseudomonas Gram-negative: ertapenem (IV or IM)
 Follow up on susceptibilities to ensure adequate coverage, particularly if the patient has a history of MDR organism



Prescribing Pearls:

- Antibiotic selection should be individualized and based on patient’s allergy, adherence history, pattern of resistance, cost, and side effects.
- Urine culture may not be needed for simple cystitis. Should always obtain urinalysis and urine culture for pyelonephritis symptoms, recent treatment, frequent recurrent urinary symptoms, or past resistant organism.
- UTI with associated conditions (poorly controlled diabetes, pregnancy, hospital-acquired infection, acute or chronic kidney injury, presence of indwelling catheter, stent, nephrostomy tube, or urinary diversion, functional or anatomic abnormality of urinary tract, renal transplant, or other immunocompromising condition) increases the risk of failing therapy.
- Broader therapy with one of the agents listed for pyelonephritis may be warranted if there is suspicion for infection with a resistant organism.
- If Pseudomonas aeruginosa is suspected, higher doses of piperacillin/tazobactam (4.5 gram IV every 6 hours with traditional infusion or 4.5 gram IV every 8 hours with extended infusion) or meropenem (1 gram every 8 hours) can be used in normal kidney function.
- Patients who initially receive IV antibiotics can transition to oral therapy when clinically stable and susceptibilities are known. Duration of IV therapy should count towards total duration of therapy.

Antibiotic Considerations in pregnancy:

- **Beta- lactams:** (amoxicillin/clavulanate, cephalexin, cefpodoxime)- Generally considered safe at all stages of pregnancy.
- **Fosfomycin:** Crosses the placenta. Generally considered safe at all stages of pregnancy.
- **Nitrofurantoin:** Avoid use during 3rd trimester, contraindicated at term. Generally safe in 1st and 2nd trimester.
- **Trimethoprim/Sulfamethoxazole:** Avoid use in 1st & 3rd trimester. Crosses placenta, can be considered if limited options exist.

Doses of oral antibiotics commonly used in treating UTI (listed alphabetically)

Drug Name	Estimated CrCl (mL/min)	Recommended Dose
Amoxicillin/clavulanic acid	CrCl ≥ 30 CrCl 10-30 CrCl < 10 ESRD on HD	875 mg BID 250-500 mg BID 250-500 mg daily 250-500 mg daily (give after HD on the day of HD)
Cefdinir	CrCl ≥ 30 CrCl <30	300 mg BID 300 mg daily
Cefpodoxime	CrCl ≥ 30 CrCl < 30 ESRD on HD	Cystitis: 100 mg BID Pyelonephritis: 200 mg BID Cystitis: 100 mg daily Pyelonephritis: 200 mg daily 200 mg three times per week following HD
Ciprofloxacin (see black box warning on page 2)	CrCl ≥30 CrCl < 30 ESRD on HD	Cystitis: 250 mg BID Pyelonephritis: 500 mg BID Cystitis: 250 mg daily Pyelonephritis: 500 mg daily 250-500 mg daily (give after HD on the day of HD)
Fosfomycin	-	3 gram in 3-4 oz. of water as single dose
Levofloxacin (see black box warning on page 2)	Simple cystitis and no suggestion of pyelonephritis CrCl ≥ 20 CrCl <20 ESRD on HD Not Simple cystitis e.g. acute uncomplicated pyelonephritis: CrCl ≥ 50 CrCl 20-49 CrCl <20 ESRD on HD	250 mg daily No adjustment required (may consider 250 mg Q48H) 250 mg Q48H 750 mg daily 750 mg Q48H 750 mg once, followed by 500 mg Q48H 750 mg once, followed by either 500 mg Q48H or 250 mg Q24H
Nitrofurantoin	CrCl ≥ 60 CrCl 30-59 CrCl <30	100 mg BID (for Macrobid®) OR 50-100 mg Q6H (for Macrochantin®) Although contraindicated in manufacturer’s labeling, data suggest nitrofurantoin is safe and effective for short-term treatment of uncomplicated cystitis (no dose adjustment required) Avoid use
Trimethoprim/ Sulfamethoxazole	CrCl > 30 CrCl 15-30 CrCl < 15	160 mg/800 mg (Bactrim DS tab) Q12H 80 mg/400 mg (Bactrim SS tab) Q12H Not recommended



Doses of intravenous antibiotics used in treating UTI (patients with simple cystitis who are unable to tolerate oral agents and patients with urinary tract infection that is not simple cystitis e.g. pyelonephritis) listed alphabetically

Drug Name	Estimated CrCl (mL/min)	Recommended Dose
Aztreonam (Use only if SEVERE beta lactam allergy)	CrCl ≥30 CrCl 10-30 CrCl < 10 IHD (assumption of 3 times/week complete hemodialysis) Peritoneal dialysis Continuous renal replacement therapy (CRRT)	1 gram IV Q8H 500 mg Q8H 250 mg Q8H Loading dose of 2 gram followed by 500 mg Q8H 1 gram Q24H CVVH: loading of 2 gram ONCE, followed by 1 -2 gram IV Q12H CVVHD/CVVHDF: loading of 2 gram ONCE, followed by either 1 gram Q8H or 2 gram Q12H
Cefepime	CrCl > 60 CrCl 30-60 CrCl 10-29 CrCl < 10 IHD (assumption of 3 times/week complete hemodialysis) Peritoneal dialysis Continuous renal replacement therapy (CRRT)	1 gram IV Q8H 1 gram IV Q12H 1 gram IV Q24H 500 mg IV Q24H Either 1 gram on day 1 followed by 500 mg IV Q24H, 1 gram Q24H, or 2 gram three times weekly after dialysis 1 gram Q24H CVVH: loading of 2 gram ONCE, followed by 1 -2 gram IV Q12H CVVHD/CVVHDF: loading dose of 2 gram ONCE, followed by 1 gram Q8H
Ceftazidime/avibactam	CrCl >50 CrCl 31-50 CrCl 16-30 CrCl 6-15 CrCl ≤ 5 ESRD on IHD	2.5 gram IV Q8H 1.25 gram IV Q8H 0.94 gram IV Q12H 0.94 gram IV Q24H 0.94 gram IV Q48H Administer based upon patient’s estimated renal function (i.e. CrCl 6-15 ml/min or CrCl ≤ 5 ml/min)
Ceftolozane/tazobactam	CrCl > 50 CrCl 30-50 CrCl 15-29 CrCl < 15, not on dialysis ESRD on IHD	1.5 gram IV Q8H 750 mg IV Q8H 375 mg IV Q8H There is no dosage adjustment provided in the manufacturer’s labeling 750 mg IV ONCE, followed by 150 mg IV Q8H
Ceftriaxone	-	1 gram IV Q24H
Ciprofloxacin (see black box warning on page 2)	CrCl ≥30 CrCl < 30	400 mg IV Q12H 400 mg IV Q24H
Doripenem (NON-FORMULARY at HMC)	CrCl > 50 CrCl 30-50 CrCl 11-29 ESRD on IHD Peritoneal dialysis Continuous renal replacement therapy (CRRT)	500 mg IV Q8H 250 mg IV Q8H 250 mg IV Q12H 250 mg IV Q24H If treating <i>Pseudomonas aeruginosa</i> , administer 500 mg IV Q12H on day 1, followed by 500 mg IV Q24H There is no dosage adjustment provided in the manufacturer’s labeling CVVHD: 1000 mg IV Q8H CVVHDF: 250 mg IV Q12H
Ertapenem	CrCl > 30 CrCl ≤ 30 and ESRD CAPD	1 gram IV Q24H 500 mg IV Q24H 500 mg IV Q24H



Continued from page 4

Drug Name	Estimated CrCl (mL/min)	Recommended Dose
Imipenem-cilastatin (NON-FORMULARY at HMC)	CrCl ≥ 60 CrCl ≥ 30 to < 60 CrCl ≥ 15 to < 30 CrCl < 15 ESRD on IHD (assumption of 3 times/week complete hemodialysis) Continuous renal replacement therapy (CRRT)	500 mg IV Q6H 500 mg IV Q8H 500 mg IV Q12H Do not administer imipenem unless hemodialysis is instituted within 48 hours Use the recommendation for patients with CrCl ≥ 15 to < 30; administer dose after dialysis session and at intervals timed from the end of that dialysis session CVVH: 1 gram ONCE, followed by either 250 mg IV Q6H – OR – 500 mg IV Q8H CVVHD: 1 gram ONCE, followed by either 250 mg IV Q6H – OR – 500 mg IV Q6-8H CVVHDF: 1 gram ONCE, followed by either 250 mg IV Q6H – OR – 500 mg IV Q6H
Levofloxacin (see black box warning on page 2)	CrCl ≥ 50 CrCl 20-49 CrCl <20 ESRD on HD	750 mg daily 750 mg Q48H 750 mg once, followed by 500 mg Q48H 750 mg once, followed by either 500 mg Q48H or 250 mg Q24H
Meropenem	CrCl > 50 CrCl 26-50 CrCl 10-25 CrCl < 10 IHD (assumption of 3 times/week complete hemodialysis) Continuous renal replacement therapy (CRRT)	500 mg IV Q6H 500 mg IV Q8H 500 mg IV Q12H 500 mg IV Q24H 500 mg IV Q24H CVVH: 1 gram ONCE, followed by either 500 mg IV Q8H – OR – 1 gram IV Q8H to 12H CVVHD/CVVHDF: 1 gram ONCE, followed by either 500 mg IV Q6
Piperacillin/tazobactam (extended infusion dosing with infusion time over 4 hours) **PREFERRED DOSING AT HMC**	CrCl > 40 CrCl 20-40 CrCl < 20 Peritoneal dialysis ERSD on HD (assumption of 3 times/week complete hemodialysis) Continuous renal replacement therapy (CRRT)	3.375 gram IV Q8H (if treating <i>Pseudomonas aeruginosa</i> , the dose is 4.5 gram IV Q8H) 3.375 gram IV Q8H (if treating <i>Pseudomonas aeruginosa</i> , the dose is 4.5 gram IV Q8H) 3.375 gram IV every 12 hours (if treating <i>Pseudomonas aeruginosa</i> , the dose is 4.5 gram IV Q12H) 4.5 gram IV every 12 hours Not applicable; Use traditional intermittent infusion dosing CVVHDF: 4.5 gram IV every 8 hours
Piperacillin/tazobactam (traditional intermittent infusion dosing with infusion time over 30 minutes)	CrCl > 40 CrCl 20-40 CrCl < 20 ESRD on HD (assumption of 3 times/week complete hemodialysis) Continuous renal replacement therapy (CRRT)	3.375 gram IV Q6H (if treating <i>Pseudomonas aeruginosa</i> , the dose is 4.5 gram IV Q6H) 2.25 gram IV Q6H (if treating <i>Pseudomonas aeruginosa</i> , the dose is 3.375 gram IV Q6H) 2.25 gram IV Q8H (if treating <i>Pseudomonas aeruginosa</i> , the dose is 2.25 gram IV Q6H) 2.25 gram IV Q8H CVVH: 2.25 to 3.375 gram IV Q6 to Q8H CVVHD: 2.25 to 3.375 gram IV Q6H CVVHDF: 3.375 gram IV Q6H



References:

- Detweiler K, et.al. Bacteriuria and urinary tract infections in the elderly. *Urol Clin N Am* 2015;42:561-568
- Ferroni M and Taylor AK. Asymptomatic bacteriuria in noncatheterized adults. *Urol Clin N Am* 2015;42:537-545
- Gupta K, et.al. International Clinical Practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52(5):e103-e120
- 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;50:625-663
- Matthews SJ and Lancaster JW. Urinary tract infections in the elderly population. *Am J Geriatr Pharmacother* 2011;9:286-309
- Nicolle LE, 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
- Robinson D, et.al. The management of urinary tract infections in octogenarian women. *Maturitas* 2013;343-347
- Lexi-Comp. 2022
- Micromedex. 2022
- Milton S Hershey Medical Center Guide to Antimicrobial Therapy 2020-2021.
<https://infonet.pennstatehershey.net/documents/596222/596226/Guide+to+Antimicrobial+Therapy+at+Hershey+Medical+Center.pdf/90d6a077-ce1e-7f8d-c67c-2d6ba7b25b5a>
- Hooton TM. Acute complicated cystitis and pyelonephritis. UpToDate. Updated Mar 2017
- Hooton TM and Gupta K. Acute uncomplicated cystitis and pyelonephritis in women. UpToDate. Updated Mar 2017
- Penn State Health Pharmacy Administration Manual: Patient Care Clinical Services Extended Infusion Beta Lactams. Policy number: 423 PAM. Last updated: March 2018

Revised: May 10, 2022	Authors: Joy Trout, PharmD, William Curry, MD, Todd Felix, MD, Michael Katzman, MD, Shawn Phillips, MD, Sesilya Whaley, PharmD
------------------------------	---