Urinary Tract Infections in Primary Care and Long Term Care

B.C. Provincial Academic Detailing Service April 2016

Acute uncomplicated cystitis non-pregnant females

- **Cystitis** is an infection of the lower urinary tract which causes dysuria ± frequency, urgency, suprapubic pain[1]
- **Acute dysuria** (< 1 week) is the most discriminating symptom of UTI in older women[1]
- **Urinalysis** (dipstick or microscopy) is a highly sensitive test in symptomatic, premenopausal women → Cystitis is unlikely if the urinalysis is negative for pyuria[1,2]
- **Pre-treatment urine cultures** are recommended if:[1]
  - Quinolone or cephalosporin use within past 6 months
  - Travel outside Canada/United States within past 6 months
  - Recent hospitalization or related healthcare exposure
  - Previous UTI with gram negative organism other than *E. coli*
  - Previous UTI with ESBL or AmpC-producing organism
  - Inadequate response to empiric therapy after 48 hours
- **Post-treatment urine cultures** are not routinely recommended after successful treatment of cystitis[1]
- **Diagnostic uncertainty** regarding cystitis versus early pyelonephritis → Avoid antibiotics that may not achieve adequate serum or renal tissue levels (nitrofurantoin, fosfomycin, cephalexin)[1,3]
- **Blood cultures** & empiric therapy for pyelonephritis are recommended if febrile[1]

Empiric oral antibiotic options[1,2,3]

nitrofurantoin 50 mg (or 100 mg) QID or MacroBID® 100 mg BID x 5 days

Alternatives

fosfomycin 3 grams x 1 dose
trimethoprim–sulfamethoxazole one DS (160/800 mg) tab BID x 3 days
ciprofloxacin 250 mg BID (or 500 mg XL once a day) x 3 days
cephalexin 500 mg QID x 5-7 days

Complicated urinary tract infection older adults, long term care

- **Older adults** → A positive urinalysis or urine culture does not reliably differentiate UTI from asymptomatic bacteriuria[1,2,4,5]
  - See *Understanding Asymptomatic Bacteriuria* Newsletter and *Urinary Tract Infections in LTCF Checklist*[5]
- **Pre-treatment urinalysis & urine cultures** are recommended if a UTI is strongly suspected[1,4,5]
- **Blood cultures** & initial intravenous antibiotic therapy are recommended if febrile, systemically unwell, or if signs & symptoms of upper UTI[1]
- **Limit duration** of antibiotic therapy to 7 days if lower UTI & prompt response to antibiotic therapy within 48 hours[1,5]
- **Post-treatment urine cultures** are not routinely recommended if clinical improvement[5]
- **Empiric antibiotic options** for UTIs are more limited in older adults living in long term care due to:[1,4,5]
  - Increased uropathogen resistance → In older adults in B.C., up to 50% of *E. coli* urinary isolates are resistant to ciprofloxacin[6]
  - Greater variability of possible uropathogens
  - Increased likelihood of complicated UTI (i.e., functional & anatomical abnormalities of the genitourinary tract)
- **Long term antibiotic** prophylaxis regimens are not recommended[5]

Empiric oral antibiotic options[1,2,4]

amoxicillin–clavulanic acid 875/125 mg BID (or 500/125 mg TID) x 7-14 days

cefixime 400 mg once a day x 7-14 days

trimethoprim–sulfamethoxazole one DS (160/800 mg) tab BID x 7-14 days

Reviewed by: Provincial Antimicrobial Clinical Expert (PACE) Group. **For more information on the management of urinary tract infections:** 1) Blondel-Hill E, Fryters S. Bugs & Drugs. http://www.bugsanddrugs.ca/; 2) Vancouver Coastal Health Antimicrobial Stewardship Programme: VCH Management of Urinary Tract Infections (UTI) in Non-Pregnant Adults; 3) Infectious Diseases Society of America *Clin Infect Dis* 2011;52(5):e103-e120; 4) Providence Health Care Antimicrobial Stewardship Program: Diagnosis & Management of Urinary Tract Infection (UTI) in Residential Care; 5) Toward Optimized Practice Diagnosis and Management of Urinary Tract Infection in Long Term Care Facilities; **Data source:** 6) LifeLabs Medical Services Proportion of *Escherichia coli* urinary isolates non-susceptible to ciprofloxacin by age of patient (2007-2014).

Oral Antibiotic	Selected clinical considerations
nitrofurantoin[1-6] (Macrodantin, generics; MacroBID) **$8** MacroBID 100 mg BID x 5 days	**limited indication:** acute uncomplicated urinary tract infection; **renal:** avoid if CrCl 40-60 mL/min;[2-5] **urine discolouration:** rust yellow to brown; **pulmonary:** acute, subacute, chronic hypersensitivity (cases of diffuse interstitial pneumonitis, pulmonary fibrosis with long term therapy); **neurologic:** cases of peripheral neuropathy including optic neuritis; **drug absorption:** increased with food
fosfomycin[7,8] (Monurol) **$14** 3 grams x 1 dose	**limited indication:** acute uncomplicated urinary tract infection; **renal:** renal impairment prolongs elimination but no dose adjustment recommended with single dose oral therapy;[7] **most common adverse events:** diarrhea, headache, vaginitis, nausea; **single dose sachet:** add to 125 mL (1/2 cup) cold water, stir to dissolve, take immediately (orange/mandarin flavour), urine concentrations maintained for 72-84 hours with single oral dose; **DDIs:** metoclopramide
trimethoprim–sulfamethoxazole[1,6,9-12] (Bactrim, Septra, generics) **$1** one DS (160/800 mg) tab BID x 3 days	**renal:** CrCl 15-30 mL/min ↓ dose to single strength tab (80/400 mg) BID, avoid if CrCl < 15 mL/min, adequate fluid intake to reduce crystalluria risk;[9] **hyperkalemia risk factors:** renal insufficiency, hypoaldosteronism, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, potassium sparing diuretics; **blistering cutaneous disorders:** erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis; **phototoxicity:** clothing & sunscreen protection; **hematologic:** contraindicated megaloblastic anemia due to folate deficiency, risk of hemolysis in glucose-6-phosphate dehydrogenase deficiency; **DDIs:** leucovorin, methenamine, methotrexate, phenytoin, fosphenytoin, warfarin, strong CYP2C9 inducers & inhibitors, strong CYP3A4 inducers
ciprofloxacin, ciprofloxacin extended release[1,6,12-17] (Cipro, generics; Cipro XL) **$4** 250 mg BID x 3 days **$10** 500 mg XL once a day x 3 days	**renal:** CrCl ≤ 30 mL/min max dose 250 mg BID or 500 mg XL once a day, adequate fluid intake to reduce crystalluria risk;[13,14] **musculoskeletal:** tendinitis, tendon rupture (increased risk age > 60, corticosteroids, strenuous physical activity, renal failure, previous tendon disorder, kidney/heart/lung transplant recipients), exacerbation muscle weakness in myasthenia gravis; **neurologic:** seizures, toxic psychosis, increased intracranial pressure, polyneuropathy; **phototoxicity:** clothing & sunscreen protection; **endocrine:** hyperglycemia or hypoglycemia; **QTc prolongation**: concomitant medications that prolong QT and/or cause torsades de pointes, see: https://www.crediblemeds.org/; **DDIs:** duloxetine, pomalidomide, tizanadine, didanosine, erlotinib, theophylline, warfarin, CYP1A2 substrates, multivalent cations
cephalexin[1,6,18,19] (Keflex, generics) **$10** 500 mg QID x 5 days	**renal:** CrCl 10-50 mL/min ↑ interval to every 8-12 hours, CrCl < 10 mL/min ↑ interval to every 12-24 hours;[19] **hypersensitivity:** inquiry for previous reactions to penicillins or cephalosporins; **drug absorption:** increased on empty stomach; **DDIs:** zinc-containing multivitamin, multiminerals
amoxicillin–clavulanic acid[1,6,20,21] (Clavulin, generics) **$8** 875/125 mg BID x 7 days	**broad spectrum:** reserved for conditions where the possibility of resistant uropathogens is increased; **renal:** CrCl 10-30 mL/min ↓ dose to 500/125 mg BID, CrCl < 10 mL/min ↓ dose to 500/125 mg once a day;[21] **hypersensitivity:** inquiry for previous reactions to penicillins or cephalosporins; morbilliform rash in patients with mononucleosis; **gastrointestinal:** diarrhea, nausea, vomiting; diarrhea slightly less frequent with 875/125 mg BID versus 500/125 mg TID; **DDIs:** warfarin
cefixime[22] (Suprax, generics) **$24** 400 mg once a day x 7 days	**broad spectrum:** reserved for conditions where the possibility of resistant uropathogens is increased; **renal:** CrCl 20-40 mL/min ↓ dose to 300 mg once a day, CrCl < 20 mL/min ↓ dose to 200 mg once a day;[22] **hypersensitivity:** inquiry for previous reactions to penicillins or cephalosporins; **most common adverse events:** diarrhea, headache, nausea, abdominal pain

Antibiotic Recommendations for Urinary Tract Infection in Pregnancy: refer to Blondel-Hill E, Fryters S. Bugs & Drugs. http://www.bugsanddrugs.ca/.
Drug Interactions (DDIs): not an exhaustive list; identifies interactions of highest relevance in Lexicomp Online and Health Canada product monographs.[1,2,3,7,9,13,14,18,20,22]
Hormonal Contraceptives: absence of high-quality evidence to confirm or refute clinical relevance or predictability of an interaction with hormonal contraceptives & antibiotics;[23-31] current estrogen-containing contraceptive monographs indicate the possibility of decreased contraceptive efficacy with several antibiotics & recommend an additional or alternative contraceptive method;[23-26] others advise that additional precautions are only required with hormonal contraceptives (including progestin-only) if the antibiotic is an enzyme inducer (such as rifampin).[27,28,30,31]
Cost: approximate medication cost without markup or professional fee, calculated from McKesson Canada: https://www.mckesson.ca/, accessed April 13, 2016.