

EMLc
Codes ATC: J01EE01

Indication	Infectious cystitis <span>Code ICD11: GC80.1</span>
INN	Sulfamethoxazole + trimethoprim
Type de médicament	Chemical agent
Groupes d'antibiotiques	<span>▼ ACCESS</span>
Type de liste	Liste de base single agent trimethoprim may be an alternative for lower urinary tract infection.
Formulations	Parenteral > General injections > IV: 80 mg + 16 mg per mL in 10 mL ampoule ; 80 mg + 16 mg per mL in 5 mL ampoule Oral > Liquid: 200 mg + 40 mg per 5 mL oral liquid Oral > Solid: 100 mg + 20 mg tablet ; 400 mg + 80 mg tablet ; 800 mg + 160 mg tablet
Historique des statuts LME	Ajouté pour la première fois en 2017 (TRS 1006)
Sexe	Tous
Âge	Aussi recommandé pour les enfants
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite <a href="#">sur les brevets.</a> 
Wikipédia	<a href="#">Sulfamethoxazole + trimethoprim</a> 
DrugBank	<a href="#">Sulfamethoxazole</a>  , <a href="#">Trimethoprim</a> 

## Recommandation du comité d'experts

The Expert Committee endorsed the inclusion of the following medicines as first-choice therapies on the EML and EMLc list: • lower UTI: amoxicillin or amoxicillin + clavulanic acid or sulfamethoxazole + trimethoprim or nitrofurantoin • pyelonephritis or prostatitis, mild to moderate: ciprofloxacin • pyelonephritis or prostatitis, severe: ceftriaxone or cefotaxime. The Expert Committee endorsed the inclusion of the following medicines as second-choice therapies on the EML and EMLc list: • pyelonephritis or prostatitis, mild to moderate: ceftriaxone or cefotaxime. The Committee recommended the addition of amikacin (in combination with ceftriaxone or cefotaxime) for severe pyelonephritis or prostatitis to the EML and EMLc for UTI therapy.

## Contexte

Urinary tract infections (UTI) in the outpatient setting are a common reason for young women in particular to seek medical attention. Randomized controlled trials (RCTs) have addressed the type and duration of antibiotic treatments in this and other populations. Use of antibiotics for asymptomatic bacteriuria can drive antibiotic resistance and may also increase the risk for subsequent symptomatic UTI. While it is accepted practice that asymptomatic bacteriuria should be treated in pregnant women and in men about to undergo urological procedures, the benefits of therapy in other groups have been questioned and addressed in RCTs.

## Résumé des preuves

A 2010 Cochrane systematic review (21 RCTs; 6016 participants) of acute uncomplicated UTI, found that sulfamethoxazole + trimethoprim (SMX-TMP) was equivalent to fluoroquinolones in achieving short-term (risk ratio (RR) 1.00; 95% confidence interval (CI) 0.97–1.03) and long-term (RR 0.99; 95% CI 0.94–1.05) symptomatic cure. Beta-lactam drugs were similar to SMX-TMP for short-term (RR 0.95, 95% CI 0.81 to 1.12) and long-term (RR 1.06, 95% CI 0.93 to 1.21) symptomatic cure but criteria for equivalence were not met (1). Short-term cure with nitrofurantoin was similar to that with SMX-TMP (RR 0.99; 95% CI 0.95–1.04) as was long-term symptomatic cure (RR 1.01; 95% CI 0.94–1.09). For asymptomatic bacteriuria, a 2015 Cochrane review of nine RCTs (1614 participants) that compared antibiotics with placebo/no treatment showed that symptomatic UTI (RR 1.11; 95% CI 0.51–2.43), complications (RR 0.78; 95% CI 0.35–1.74) and death (RR 0.99; 95% CI 0.70–1.41) were similar in the two treatment arms (2). A 2014 Cochrane review of antibiotics for pyelonephritis in children (27 studies; 4452 children) reported no significant differences in duration of fever (2 studies; 808 children; mean difference (MD) 2.05 hours; 95% CI –0.84 to 4.94), persistent UTI at 72 hours after start of therapy (2 studies; 542 children; RR 1.10; 95% CI 0.07–17.41) or persistent kidney damage at 6–12 months (4 studies; 943 children; RR 0.82; 95% CI 0.59–1.12) between oral antibiotic therapy (10–14 days) and IV therapy (3 days) followed by oral therapy (10 days) (3). Similarly, there were no significant differences in persistent bacteriuria at the end of treatment (4 studies; 305 children; RR 0.78; 95% CI 0.24–2.55) or persistent kidney damage (4 studies; 726 children; RR 1.01; 95% CI 0.80–1.29) between IV therapy (3–4 days) followed by oral therapy and IV therapy (7–14 days) (3). No significant differences in efficacy were found between daily and three times daily administration of aminoglycosides (1 study; 179 children; persistent clinical symptoms at three days: RR 1.98; 95% CI 0.37–10.53).

## Recommandations

The Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines recommend nitrofurantoin and SMX-TMP for acute uncomplicated cystitis in women (4). Amoxicillin + clavulanic acid is an alternative choice. Oral fosfomicin is recommended where available because of its minimal propensity for resistance. Ceftriaxone is recommended for acute pyelonephritis in women, as is ciprofloxacin. However, the guideline recommends that resistance rates for empirically selected antibiotics should be below 10% for pyelonephritis and below 20% for treatment of lower UTI, a threshold no longer met for fluoroquinolones in many countries. Amoxicillin + clavulanic acid and SMX-TMP are also recommended for empirical treatment in children aged 2–24 months by the American Academy of Pediatrics (5). The European Association of Urology and European Society for Paediatric Urology state that antimicrobial choice is dictated by local resistance patterns (6). For young children, newborns and infants, parenteral therapy is advised, such as combination treatment with ampicillin and an aminoglycoside (e.g. tobramycin or gentamicin) or a third-generation cephalosporin. For pyelonephritis during the first 6 months of life, ceftazidime plus ampicillin or an aminoglycoside plus ampicillin is recommended. A third-generation cephalosporin is recommended for children over 6 months of age for uncomplicated pyelonephritis while ceftazidime plus ampicillin or aminoglycoside plus ampicillin are suggested for complicated pyelonephritis. Although the guidelines list parenteral as well as oral cephalosporins, in addition to beta-lactams (including piperacillin, amoxicillin, amoxicillin + clavulanic acid, nitrofurantoin and aminoglycosides), fluoroquinolones are considered second- or third-line antibiotics for complicated urinary tract infection. The recommendations of the Italian Society for Pediatric Nephrology are similar (7).

## Justification de la sélection des antibiotiques

The systematic review evidence showed that SMX-TMP was equivalent to fluoroquinolones for uncomplicated UTI and that nitrofurantoin was equivalent to SMX-TMP. SMX-TMP and nitrofurantoin are therefore proposed as core antibiotics. Fluoroquinolones were not included because of the need to preserve this class of antibiotics. Oral fosfomicin is proposed because of minimal resistance and good safety profile. Amoxicillin + clavulanic acid is proposed for young children while ampicillin and gentamicin are for children with severe illness. Fosfomicin is included as a core antibiotic.

## Considérations du comité

For common community-acquired infections, the main focus has been on empirical treatment choices that are broadly applicable in most countries. Generally, alternatives for use in case of allergy were not considered. The Expert Committee considered the various antibiotics proposed in the application under the guiding principle of parsimony and selected first- and second-choice antibiotics for this indication for inclusion on the EML and/or EMLc. Ampicillin, fosfomicin and gentamicin were excluded. Amikacin was preferred to gentamicin because it is generally more active on Enterobacteriaceae; ciprofloxacin was added as a recommended

first-line option for empirical treatment in mild-to-moderate pyelonephritis and prostatitis because of its good bioavailability and penetration (if local/national epidemiological data allow). Recommended first- and second-choice antibiotics are reported above. The first-choice antibiotics are those generally recommended on the basis of available evidence and are usually narrow-spectrum agents.

## Recommandations de la LME : Infectious cystitis

### Premier choix

nitrofurantoin

amoxicillin

amoxicillin + clavulanic acid

sulfamethoxazole + trimethoprim

### Second choix

1. Zalmanovici Trestioreanu A, Green H, Paul M, Yaphe J, Leibovici L. Antimicrobial agents for treating uncomplicated urinary tract infections. *Cochrane Database Syst Rev*.
2. Zalmanovici Trestioreanu A, Lador A, Sauerbrun-Cutler MT, Leibovici L. Antibiotics for asymptomatic bacteriuria. *Cochrane Database Syst Rev*.
3. Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev*.
4. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women. *Am J Med*.
5. Roberts KB, Subcommittee on Urinary Tract Infection Steering Committee on Quality Improvement and Management. Urinary tract infections in children: AAP clinical practice guideline. *Pediatrics*.
6. Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C et al. Urinary tract infections in children: EAU/ESPU guidelines. *EAU Guidelines on Urinary Tract Infections*.
7. Ammenti A, Cataldi L, Chimenz R, Fanos V, La Manna A, Marra G et al. Febrile urinary tract infections in young children: recommendations for empirical treatment. *Paediatr Child Health*.

