

Implementing the NICE guidance for urinary tract infection (lower): antimicrobial prescribing¹ for non-pregnant women without a catheter aged 16 years and over^[A]

[A] Refer to the NICE NG109 guideline¹ for the full guidance.

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Lower urinary tract infection (UTI)

- Lower UTI is an infection of the bladder, also referred to as cystitis
- It is usually caused by gastrointestinal tract bacteria (most commonly *Escherichia coli*) entering the urethra and travelling up to bladder
- Antibiotic use should be optimised to reduce antibiotic resistance.

Self care advice (offer to all women with UTI)

- Use paracetamol for pain or ibuprofen if suitable and preferred
- Ensure enough fluids are drunk to avoid dehydration
- Guidance states there is a lack of evidence using cranberry products or alkalinising agents to treat lower UTI.

Treatment for non-pregnant women aged ≥ 16 years with lower UTI

Consider a back-up antibiotic prescription (to use if symptoms do not start to improve within 48 hours or worsen at any time) or an immediate antibiotic prescription (offer advice of possible adverse effects of the antibiotic, particularly diarrhoea and nausea and seeking medical help if symptoms worsen rapidly or significantly at any time, do not start to improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell)

Take account of:

the risk of developing complications, which is higher in people with known or suspected structural or functional abnormality of the genitourinary tract or immunosuppression

the severity of symptoms

previous urine culture and susceptibility results

previous antibiotic use, which may have led to resistant bacteria

preferences of the woman for antibiotic use

local antimicrobial resistance data

refer people aged >16 years with lower UTI to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, sepsis).

Choice of antibiotic

First choices

Nitrofurantoin if eGFR ≥ 45 ml/minute 100 mg modified release (MR) twice daily or 50 mg four times daily for 3 days

Trimethoprim 200 mg twice daily for 3 days if low risk resistance (refer to antimicrobial resistance (AMR) local indicators).

Second choices (if no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice is not suitable)

Nitrofurantoin if eGFR ≥ 45 ml/minute 100 mg MR twice daily or 50 mg four times daily for 3 days if not used as first choice

Pivmecillinam (a penicillin) 400 mg first dose then 200 mg three times daily for a total of 3 days
Fosfomicin 3 g single dose sachet.

Monuril (fosfomicin trometerol)

- A single dose, orally administered antibiotic²
- Indicated for the treatment of acute, uncomplicated cystitis in women and female adolescents²
- Resistance rates in *E. coli* have remained low, even with widespread use in Europe for many years^{3,4}
- Demonstrated susceptibility in ESBL-producing *E. coli*⁵
- Included in NICE guidelines as a second choice, or as an alternative empirical treatment if first choice options are unsuitable.¹

Reassessment

Reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of:

- other possible diagnoses
- any symptoms or signs suggesting a more serious illness or condition, such as pyelonephritis
- previous antibiotic use, which may have led to resistant bacteria.

Send a urine sample for culture and susceptibility testing if this has not already been done and review treatment when results are available.

Prescribing Information

Monuril 3g granules for oral solution

Consult Summary of Product Characteristics before prescribing.

Legal Category: POM

Marketing Authorisation number and basic NHS cost: PL 31654/0006, £4.86 per sachet.

Presentation: One sachet contains 5.631 g of fosfomycin trometamol equivalent to 3.0 g fosfomycin

Uses: Monuril is indicated for:

- the treatment of acute, uncomplicated cystitis in women and female adolescents
- perioperative antibiotic prophylaxis for transrectal prostate biopsy in adult man

Dosage and administration:

Acute, uncomplicated cystitis in women and female adolescents (>12 years of age): 3 g fosfomycin once

Perioperative antibiotic prophylaxis for transrectal prostate biopsy: 3 g fosfomycin 3 hours prior to the procedure and 3 g fosfomycin 24 hours after the procedure.

Method of administration

For oral use. For the indication of acute, uncomplicated cystitis in women and female adolescents it should be taken on an empty stomach (about 2-3 hours before or 2-3 hours after a meal), preferably before bedtime and after emptying the bladder. The dose should be dissolved into a glass of water and taken immediately after its preparation.

Special populations:

Children: The safety and efficacy of Monuril in children below 12 years of age have not been established. Therefore, this medicine should not be used in this age group.

Renal impairment: In patients with impaired renal function, the elimination half-life is increased proportionally to the degree of renal insufficiency. Urinary concentrations of fosfomycin in patients with impaired renal function remain effective for 48 hours after a usual dose if creatinine clearance is above 10 ml/min. In older people fosfomycin clearance is reduced in line with the age related reduction in renal function. Use of Monuril is not recommended in patients with renal impairment (creatinine clearance < 10 ml/min).

Pregnancy: Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Monuril should only be used during pregnancy, if clearly necessary.

Breastfeeding: Fosfomycin is excreted in human milk in low quantities. If clearly necessary, a single dose of oral fosfomycin can be used during breast-feeding.

References:

1. NICE. *Urinary tract infection (lower): antimicrobial prescribing*. NICE guideline NG109. NICE, 2018. Available at: www.nice.org.uk/guidance/ng109
2. Profile Pharma Limited. *Monuril 3g granules for oral solution—summary of product characteristics*. May 2021. www.medicines.org.uk/emc/product/7329/smpc
3. Heytens S, Boelens J, Claeys G et al. Uropathogen distribution and antimicrobial susceptibility in uncomplicated cystitis in Belgium, a high antibiotics prescribing country: 20-year surveillance. *European Journal of Clinical Microbiology & Infectious Diseases* 2016; **36** (1): 105–113.
4. Kahlmeter G and Poulsen H. Antimicrobial susceptibility of *Escherichia coli* from community acquired urinary tract infections in Europe: The ECO-SENS study revisited. *International Journal of Antimicrobial Agents* 2012; **39** (1): 45–51.
5. Raja NS. Oral treatment options for patients with urinary tract infections caused by extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae. *J Infect Public Health* 2019; **12** (6): 843–846.

Warnings and Precautions:

Serious and occasionally fatal hypersensitivity reactions, including anaphylaxis and anaphylactic shock, may occur. Clostridioides difficile-associated colitis and pseudo-membranous colitis have been reported with fosfomycin. It is important to consider this diagnosis in patients who present with diarrhoea. It may be symptomatic of Clostridium Difficile.

Monuril contains sucrose; patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not use this medicine. The presence of sulphites may cause severe hypersensitivity reactions and bronchospasm. Its use is not recommended in patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

No specific studies have been performed but patients should be informed that dizziness has been reported. This may influence some patients' ability to drive and use machines.

Contraindications:

Hypersensitivity to the active substance or to any of the excipients.

Interactions:

Concomitant administration of metoclopramide has been shown to lower serum and urinary concentrations of fosfomycin and should be avoided. Other medicinal products that increase gastrointestinal motility may produce similar effects. Food may delay the absorption of fosfomycin, with consequent slight decrease in peak plasma levels and urinary concentrations. It is therefore preferable to take the medicinal product on an empty stomach or about 2-3 hours after meals.

Side Effects:

The most common adverse reactions following the single-dose administration of fosfomycin trometamol involve the gastrointestinal tract, mainly diarrhoea. Other common undesirable effects are vulvovaginitis, headache, dizziness, nausea, dyspepsia and abdominal pain. Anaphylaxis and angioedema have been reported with an unknown frequency. Consult the summary of product characteristics for other side effects.

Further information is available from Profile Pharma Ltd, Bicentennial Building, Southern Gate, Chichester, West Sussex. P019 8EZ United Kingdom.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Profile Pharma Ltd. at profile.drugsafety@ZambonGroup.com