

Monuril®

Fosfomicyn (as Trometamol)

Adult 3g



NAME OF MEDICINAL PRODUCT: Monuril 3g granules for oral solution

(Please refer to the full Summary of Product Characteristics before Prescribing)

Each single-dose sachet contains 5.631 g fosfomicyn – trometamol (1:1) equivalent to 3g fosfomicyn. It is a white granular powder for oral solution with a characteristic odour and flavour of mandarin. **THERAPEUTIC INDICATIONS:** Treatment of acute uncomplicated urinary tract infections due to sensitive organisms in adults. **POSOLGY AND ADMINISTRATION: Adults only:** A single dose of 3g taken on an empty stomach, preferably before bedtime, after bladder emptying. The contents of the sachet should be dissolved in water and the solution swallowed immediately. **Elderly patients:** Not recommended due to diminished urinary excretion. **Paediatric population:** It is not for use in children. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. Monuril should not be used in patients with impaired renal function (creatinine-clearance <80 ml/min). **WARNINGS AND SPECIAL PRECAUTIONS FOR USE:** *Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including fosfomicyn trometamol, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*. *C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated. **This medicinal product contains sucrose.** Patients with rare hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine. **Do not use more than one single dose of Monuril to treat a single episode of acute cystitis.** Prolonged use of an anti-infective may result in the development of super infection due to organisms resistant to that anti-infective. **INTERACTIONS:** When co-administered with fosfomicyn, metoclopramide lowers the serum and urine concentrations of fosfomicyn. Other drugs that increase gastrointestinal motility may produce similar effects. Food can delay the absorption of active, therefore should be taken 2-3 hours after food. Numerous cases of increased anti vitamin K antagonists activity have been reported in patients receiving antibiotics. Risk factors include severe infection or inflammation, age and poor general health. Under these circumstances, it is difficult to determine whether the alteration in INR is due to the infectious disease or its treatment. However, certain classes of antibiotics are more often involved and in particular: fluoroquinolones, macrolides, cyclins, cotrimoxazole and certain cephalosporins. **FERTILITY, PREGNANCY AND LACTATION: Pregnancy:** At the present time, single-dose antibacterial treatments are not suitable to treat urinary tract infections in pregnant women. Animal studies do not indicate reproductive toxicity. A large amount of data concerning effectiveness of fosfomicyn during pregnancy is available. However, only moderate amount of safety data on pregnant women is available and does not indicate any malformative or fetoneonatal toxicity of fosfomicyn. **Lactation:** Fosfomicyn is excreted into human milk at low level after a single injection. Therefore Fosfomicyn can be used during breast feeding, after a single oral dose. **Fertility:** No effect on fertility has been reported in animal studies. No data are available in human **USING MONURIL WITH FOOD & DRINK:** Take Monuril on an empty stomach (2-3 hrs after a meal) as food delays and reduces the absorption of fosfomicyn trometamol, resulting in reduced blood and urinary concentrations. **DRIVING AND USING MACHINERY:** Monuril oral solution to date, has had no influence on the ability to drive and use machines. **UNDESIRABLE EFFECTS: COMMON** (≥1/100 to <1/10): Headache, Dizziness, Diarrhoea, Nausea, Vulvovaginitis, Dyspepsia **UNCOMMON** (≥ 1/1,000 to <1/100): Vomiting, abdominal pain, rash, Urticaria, Pruritus, Asthenia. **NOT KNOWN:** (<1/10,000) Anaphylactic reactions: including shock & hypersensitivity, Asthma, Antibiotic-associated colitis Angioedema, Hypotension. **OVERDOSE: Symptoms:** The following events have been observed in patients who have taken MONURIL 3 g granules for oral solution in overdose: vestibular loss, impaired hearing, metallic taste, and general decline in taste perception. Cases of hypotonia, somnolence, electrolytes disturbances, thrombocytopenia and hypoprothrombinemia have been reported with parenteral use of fosfomicyn. **Treatment in the event of overdose:** In the event of over dosage, treatment should be symptomatic and supportive. Rehydration is recommended to promote urinary elimination of the drug. **PHARMACODYNAMIC PROPERTIES:** Fosfomicyn trometamol [mono (2-ammonium-2-hydroxymethyl-1,3-propanediol) (2R-cis) (3- methoxyranil) phosphonate] is a broad spectrum antibiotic, derived from phosphonic acid, for the treatment of urinary tract infections. The antibacterial activity of fosfomicyn is due to an inhibition of bacterial cell wall synthesis. Its particular mechanism of action, specific inhibition of enol pyruvyltransferase, results in lack of cross resistance with other classes of antibiotic, and the possibility of synergism with other antibiotics (in vitro synergic effect with amoxicillin, cephalaxin, piperidic acid and aztrenam). **Pharmacokinetic properties:** Fosfomicyn trometamol which is an orally well absorbed salt of fosfomicyn, in which the formulation is completely soluble in water. Fosfomicyn, unbound to the plasma proteins, is eliminated mainly unchanged through the kidneys and this results in very high urinary concentrations (about 3000mcg/ml) within 24 hours. Therapeutic concentrations of the active moiety in the urine are usually maintained for at least 36-48 hours. In patients with moderately reduced renal function (including elderly patients) the serum half-life of fosfomicyn is slightly prolonged but urinary concentration remains therapeutically adequate. **Legal category: POM Package Quantities:** Sachets are supplied in cardboard outer containing 1 sachet

MARKETING AUTHORISATION HOLDER: Zambon S.p.A. via Lillo del duca, 10 20091-Bresso, Milano, Italy

MARKETING AUTHORISATION NUMBER: PA1441/2/2

MARKETED IN IRELAND BY: FANNIN LTD, FANNIN HOUSE, LEOPARDSTOWN, DUBLIN 18

For a copy of the SmPC or further medical information, please contact medical@dccvital.com

Adverse events should be reported to Fannin Ltd, Pharmacovigilance at 01 2907179 or medical@dccvital.com

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care professionals are asked to report any suspected adverse reactions via HPR A Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

Date of last PI revision: March 2017

IE1716/SmPC-November 2014

*Ireland: Available at <http://www.hse.ie/eng/services/list/2/gp/Antibiotic/Prescribing/Conditions-and-Treatments/Urinary/Adult-Uncomplicated-UTI/Adult-Uncomplicated-UTI.html>, Last Accessed: 05/09/2017.

Europe: Guidelines on Urological Infections (2015) M. Grabe, R. Bartoletti, T.E. Bjerklund Johansen, T. Cai, M. Çek, B. Köves, K.G. Naber, R.S. Pickard, P. Tenke, F. Wagenlehner, B. Wullt. European Association of Urology.

References:

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2. Ferrari V, Bonanomi L, Borgia M, Lodola E, Marca G. A new fosfomicyn derivative with much improved bioavailability by oral route. *Chimioterapia Antimicrobica* 1981 ; 4: 59-63.
3. Raz, R. Fosfomicyn: an old-new antibiotic. *Clinical Microbiology and Infection*. 2011 Jan; 18(1):4-7.
4. Stein GE. Comparison of single-dose fosfomicyn and a 7-day course of nitrofurantoin in female patients with uncomplicated urinary tract infection. *Clin Ther* 1999 Nov, 21(11): 11864-72.
5. Cornaglia G et al, Antibacterial Activity of Fosfomicyn Trometamol in an in vitro Model of the Urinary Bladder. *Int. Symp.*, Rome, 1987, pp. 255-260 (Karger Basel 1988).
6. Reynaert, J. Van Eyck, D. Vandepitte, J. (1990) Single dose fosfomicyn trometamol versus multiple dose norfloxacin over three days for uncomplicated UTI in general practice. *Infection*, (18:2) pp S77-S79.
7. Monuril Summary of Product Characteristics
8. Zhanel G.G et al. Fosfomicyn: A first-line Oral Therapy for acute Uncomplicated Cystitis Canadian Journal of Infectious Diseases and Medical Microbiology Vol 26.

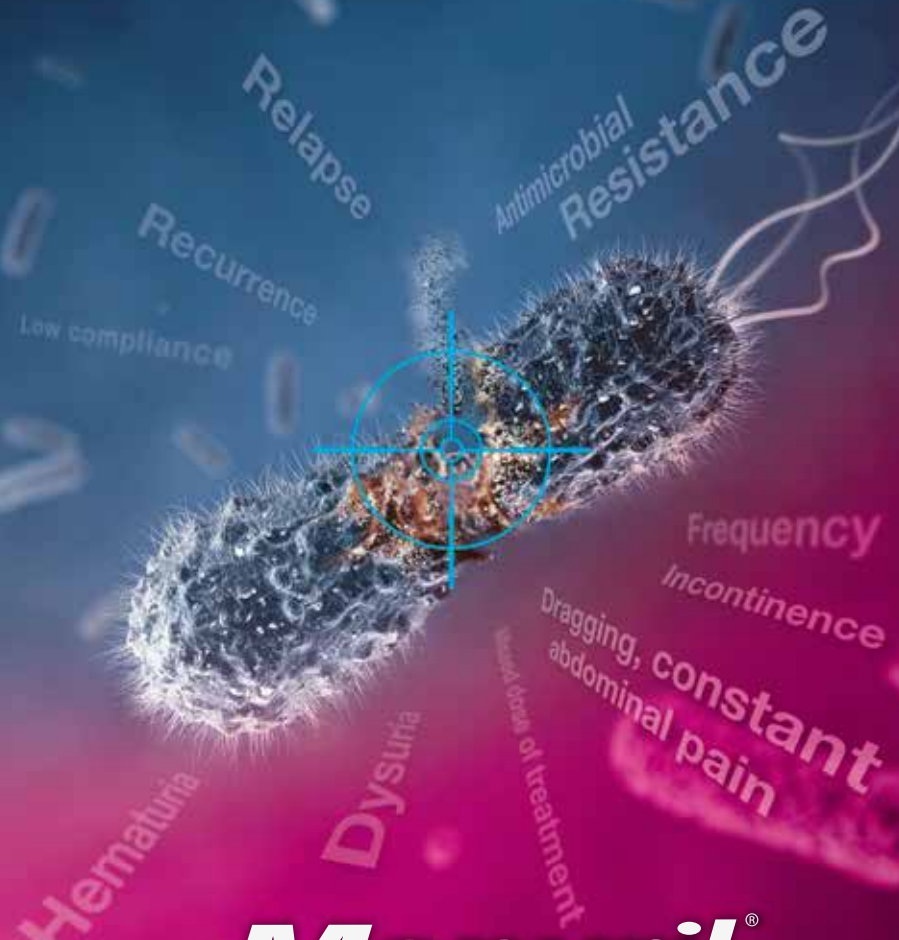


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First Line Treatment of UNCOMPLICATED UTIs*



Monuril®

Fosfomicyn (as Trometamol)

Adult 3g

Monuril®

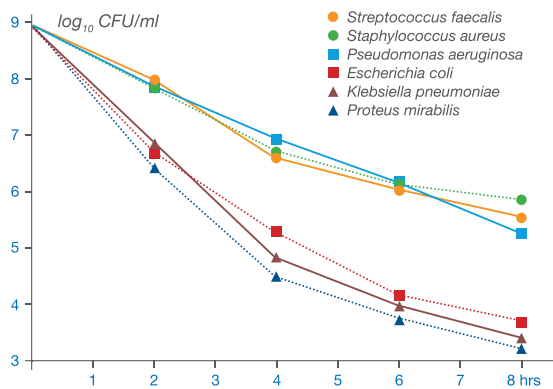
Fosfomycin (as Trometamol)

Adult 3g

An established and clinically proven Urospecific antibiotic therapy with a sustainable 3 day bactericidal action in just ONE Single Dose.

- Monuril (Fosfomycin Trometamol) is a phosphonic acid derivative with a unique mechanism of bactericidal action.¹
- The addition of Trometamol salt makes the antibiotic highly soluble and provides greatly improved bioavailability.²
- Fosfomycin Trometamol is primarily excreted unchanged in the urine.³
- Fosfomycin Trometamol is as effective and tolerable as both Trimethoprim and Nitrofurantoin.⁴

Eradication of different bacterial species using Monuril.⁵

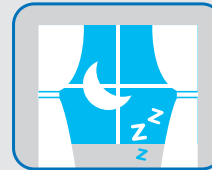


- At 4 hours, the number of *E. coli*, *Klebsiella pneumoniae* and *Proteus mirabilis* drops by 50%
- At 8 hours, more than 90% is destroyed with just ONE single dose

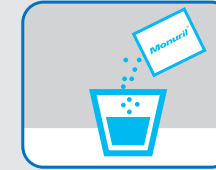
Eradication of different bacterial species using Monuril.

Fosfomycin Trometamol is the first line choice for treatment of uncomplicated UTIs in Ireland and Europe according to antimicrobial prescribing guidelines.*

Administration



Ideally, should be taken on an empty stomach, at bed time



Dissolve one sachet into a glass of water, 2-3 hours after your last meal/drink



Swallow solution

- One dose allows 100% patient compliance with treatment regime⁶
- Therapeutic concentrations reached within 2-4 hours and maintained for at least 36-48 hours⁷
- Resistance remains rare in regions where it is widely used (~2%)⁸

Advantages of a ONE Shot Treatment of Monuril®