Guidelines on the use of oral Fosfomycin 3g sachets for the treatment of multi-resistant urinary tract infections (UTIs)

Background

In recent years there has been a marked increase in the prevalence of UTIs caused by coliforms that are resistant to both penicillins and cephalosporins (i.e. extended spectrum beta lactamase [ESBL] producing organisms). Many of these organisms also carry additional resistance mechanisms which mean all currently available UK licensed oral antibiotics are ineffective.

Multi-resistant coliforms tend to occur in the elderly and in many cases bacteriuria is asymptomatic and does not require antibiotic therapy. However in patients with symptomatic or otherwise clinically significant infection, which may lead to bacteraemia, treatment is indicated. To date these patients have been treated with intravenous therapy, mainly as inpatients or on the Ambulatory Care Unit at the Great Western Hospital in Swindon.

Public Health England (PHE) now recommend if increased resistance risk and GFR<45 ml/min or elderly consider fosfomycin for treatment of UTI in adults (with no fever or flank pain).

Fosfomycin is an orally active, bactericidal antibiotic that inhibits bacterial cell wall production. It is well absorbed after oral administration (but absorption can be reduced if taken with food) and excreted unchanged in the urine. After a 3g dose, very high urine levels are achieved, urine concentrations remaining above the minimum inhibitory concentration of sensitive organisms for up to 48 hours.

Fosfomycin has been available in most of Europe, Japan and the U.S.A. for some time and a licensed 3g sachet is now available in the UK. It will now be available for dispensing on an FP10 prescription and can be provided by community pharmacies.
Prescribing Fosfomycin:

See Appendix 1: The Pathway for the Management of Community-based Patients with non-severe Urinary Tract Infections in whom Fosfomycin and/or a Carbapenem are the only treatment options

Inclusion criteria
Patients are eligible for treatment with Fosfomycin if the following criteria are fulfilled:
- They must be suffering from a symptomatic UTI.
- A urine specimen must have been examined by the laboratory.
- There must be a significant growth of a Fosfomycin-sensitive organism in the sample.
- There must be no other suitable oral treatment alternative, either because of bacterial resistance, or because of patient allergy or intolerance to suitable antimicrobials.

Prescribing information
Licensing: Acute lower uncomplicated urinary tract infection.
Dosing: Uncomplicated UTI in females – 1 x 3g sachet dissolved in a glass of water and taken immediately after meals as a single dose preferably before bedtime after emptying the bladder. Male – 1 x 3g sachet, repeat dose at Day 3 or as advised by microbiology.

Contraindications: Known hypersensitivity to fosfomycin or product excipients*
Severe renal insufficiency (CrCl < 10ml/min) or patients undergoing haemodialysis.
Suspected bacteraemia (NB: NOT recommended for ESBL pyelonephritis or peri-nephric abscess, where alternative I.V. antibiotics are required)

Cautions: Pregnancy and breast feeding (only when benefit outweighs risk).

Adverse effects: GI problems e.g. nausea, diarrhoea, headaches, vaginitis, skin rashes (self limiting), rarely hypersensitivity reactions and impairment of liver function

Drug interactions: Metoclopramide slows absorption of Fosfomycin – leave at least 2 – 3 hours between preparations or avoid metoclopramide if possible (* due to sucrose content, not recommended in patients with fructose intolerance, glucose–galactose malabsorption syndrome, or sucrase–isomaltase deficiency)

If a GP has a patient who fulfils the above criteria and Fosfomycin is the only oral option (as indicated by the microbiology report) then an appropriate dose of Fosfomycin 3g sachet should be prescribed on FP10 for dispensing at a local community pharmacy.

Appendix 1: Pathway for the Management of Community-based Patients with Urinary Tract Infections in whom Fosfomycin and/or a Carbapenem are the only treatment options

Compliance with these guidelines will be reviewed regularly by the Trust Prescribing Committee. Please check the intranet to ensure you have the latest version.

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Contact Numbers: Microbiology Ext 4800; Antibiotics Pharmacist Ext 5033; Medicines Information Ext 5029
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Discuss antibiotic options with Microbiologist (01793 604800), ensuring that you mention the following if relevant:
- allergy history
- renal impairment/ creatinine clearance
- pregnant, breast feeding
- history of seizures or pre-existing central nervous system disorders
- if taking sodium valproate, oral contraceptive pill, oral anticoagulant or metoclopramide
- on low sodium diet

Possible options are a longer Fosfomycin course or alternative IV treatment (Ertapenem or Meropenem).