The Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) have updated their guidance to allow nitrofurantoin to be prescribed to patients with reduced renal function. This change was influenced by increasing resistance to trimethoprim and amoxicillin in the UK; meaning that there is an increased need to prescribe nitrofurantoin to patients with acute cystitis. The Medicines Adverse Reactions Committee (MARC) recently discussed whether a similar change in guidance was appropriate for New Zealand.

It was concluded by MARC that the contraindication of creatinine clearance of < 60 mL/min for the use of nitrofurantoin, as listed on the New Zealand medicine datasheet, should remain. The recent Best Tests article on treating urinary tract infections (UTIs) in older people (July, 2015) reported guidance on the use of nitrofurantoin in patients with reduced renal function consistent with the UK position, i.e. avoid in patients with estimated glomerular filtration rate [eGFR] < 45 mL/min/1.73m²; this advice has now been updated in the online version of this article to account for the recent decision by MARC.

For further information, see: “A pragmatic guide to asymptomatic bacteriuria and testing for urinary tract infections (UTIs) in people aged over 65 years”, Best Tests (Jul, 2015).

The role of nitrofurantoin in the treatment of acute cystitis

Nitrofurantoin or trimethoprim are suitable first-line treatment options for non-pregnant females and males with acute cystitis. Use of nitrofurantoin can be problematic for patients with renal dysfunction. Reduced renal function may lead to toxicity due to an increase in nitrofurantoin serum levels. Impaired renal function also decreases the efficacy of nitrofurantoin as an antibacterial medicine in the urinary tract.

Serious pulmonary reactions, both acute and chronic, and which can be fatal, have been reported secondary to treatment with nitrofurantoin. The incidence of acute pulmonary reactions in patients taking nitrofurantoin is estimated to be less than 1% and it most often affects females aged 40 – 50 years. Acute pulmonary reactions are reported to occur more frequently after repeated courses of nitrofurantoin treatment.

Trimethoprim is generally considered to be better tolerated than nitrofurantoin and the dosing regimen is simpler as it is taken once daily, at night. However, antibiotic resistance levels for Escherichia coli, the most frequent cause of cystitis, are reported to be higher for trimethoprim compared with nitrofurantoin. In 2013, the percentage of urinary E. coli reported as resistant to nitrofurantoin from hospital and community laboratories was 1.3% (from almost 100 000 isolates tested). During the same period the percentage of urinary E. coli reported as resistant to trimethoprim was 26.2% (from approximately 98 000 isolates tested).

Deciding whether to prescribe trimethoprim or nitrofurantoin

The patient’s renal function, tolerance, the complexity of the dosing regimens and local bacterial susceptibility are relevant considerations when prescribing antibiotics for acute cystitis.

Comment from Associate Professor Mark Thomas, Infectious Diseases Specialist, University of Auckland:

I would recommend nitrofurantoin, 50 mg, four times daily, for five days in females and seven days in males, as the first-line treatment for uncomplicated acute cystitis in patients with creatinine clearance > 60 mL/min (avoid
in women who are 36+ weeks pregnant). In patients with renal impairment or known intolerance or allergy to nitrofurantoin, use trimethoprim 300 mg, once daily for three days in females (avoid during the first trimester of pregnancy) and seven days in males. If there is a known high rate of resistance (> 15%) to trimethoprim in E. coli in the local area, consider taking a urine sample and adjust treatment based on the susceptibility results of the organism isolated.

While norfloxacin is an alternative antibiotic for the treatment of cystitis, it should be strictly reserved for isolates resistant to trimethoprim or nitrofurantoin. Norfloxacin should be avoided in pregnant women or in patients who have severe renal impairment (refer to the New Zealand Formulary for details). For further information about the use of norfloxacin see: “Quinolone antibiotics – limit use”, BPJ 35 (Apr, 2011).

References