



# Antimicrobial Stewardship in Primary Care

## Part II: An Update on Urinary Tract Infection Management for Community Pharmacists

Welcome to the second part of a three-part series of CPD articles on antimicrobial stewardship in primary care. This instalment will focus on an update on urinary tract infection management for community pharmacists

### Introduction

The anatomical location of an infection in the urinary system is most commonly used to categorise a UTI. Infection of the urethra (urethritis), bladder (cystitis), and kidney (pyelonephritis) is one categorisation. Lower UTI (urethra or bladder) or upper UTI (ureters or kidneys) is another categorisation.

For further learning on UTIs, their causes, risk factors, prevalence, prevention, diagnosis and treatment,

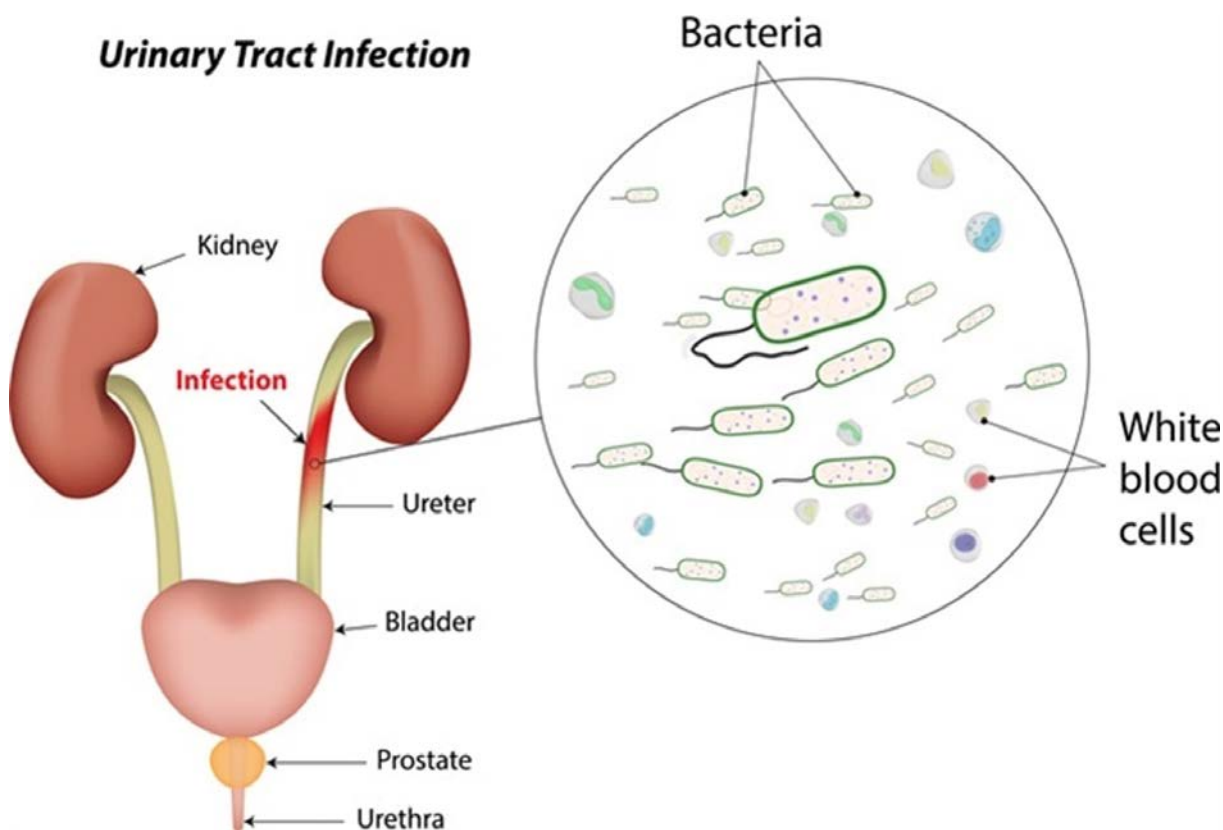
please see the course on [www.hseland.ie](http://www.hseland.ie) entitled 'Prevention and Management of Urinary Tract Infections'.

### Antibiotics used in the Treatment of UTIs

Antibiotic choice in UTI will be determined by several factors:

- Infection location: whether an agent is required for the bladder only, or whether blood levels need to be reached (systemic action);

Figure 1: A urinary tract infection is an infection of any part of the urinary system.



■ Likely (or known) causative pathogen and its susceptibility: UTIs are usually caused by bacteria that normally live in the bowel e.g. *E. coli* which is a gram-negative bacillus. Unfortunately, it is these same gram-negative bugs which are becoming increasingly resistant to antibiotics to the level of public health emergency, such as extended-spectrum beta-lactamase producing

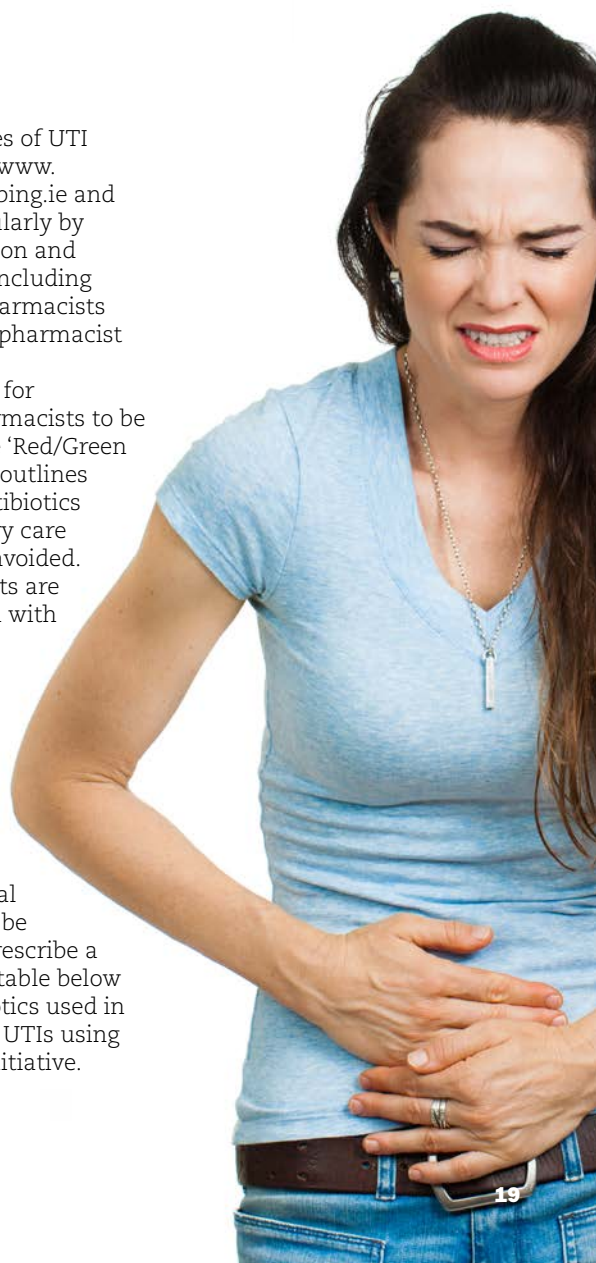
organisms (ESBL) and carbapenemase-producing enterobacteriaceae (CPE);

■ Patient factors e.g. allergy status/ drug-drug or drug-disease interactions/ previous antibiotic therapy/ pregnancy and renal function.

All of the current recommended therapies, taking into account known resistance rates, for the

various categories of UTI are available on [www.antibioticprescribing.ie](http://www.antibioticprescribing.ie) and are updated regularly by a panel of infection and clinical experts including antimicrobial pharmacists and community pharmacist representatives.

It is important for community pharmacists to be familiar with the 'Red/Green Initiative' which outlines the preferred antibiotics for use in primary care and those to be avoided. The 'Green' agents are either associated with a better adverse effect profile or less potential for promoting antimicrobial resistance compared to the 'Red' agents. However, for certain clinical scenarios it may be appropriate to prescribe a 'Red' agent. The table below describes antibiotics used in the treatment of UTIs using the Red/Green initiative.



## Remember!

The antibiotic chosen needs to eradicate the likely causative pathogen with as little influence on 'good' bacteria as possible to minimise the collateral damage from antibiotic use including development of adverse effect, secondary candida infections, *C. difficile* infection and antimicrobial resistance, i.e. an effective narrow spectrum agent is preferred to a broad spectrum agent.

**Table 1: Commonly Prescribed Antibiotics in the Treatment of UTIs**

Antibiotic	'Green'/'Red'	Commentary
<b>Nitrofurantoin</b>	<b>Green</b>	<p>Nitrofurantoin is one of the preferred agents for the treatment of uncomplicated lower UTI unless contra-indicated. Nitrofurantoin resistance rates remain relatively low amongst commonly encountered bacteria causing UTIs (including ESBL-producing isolates) despite increasing resistance to other antibiotics. Nitrofurantoin concentrates well in the bladder but is only suitable for uncomplicated <b>lower</b> urinary tract infections.</p> <p>Some practice points to be aware of with nitrofurantoin include:</p> <ol style="list-style-type: none"> <li>Tissue concentrations are too low for treatment of systemic infection, including pyelonephritis.</li> <li>Nitrofurantoin should not be used in patients with moderate-severe renal impairment because of diminished urinary tract concentrations (can't get through the kidney to the site of action) and increased risk of toxicity (systemic accumulation, with increased risk of blood dyscrasias, acute and chronic pulmonary and hepatic reactions). This is particularly important in older patients, including those in residential care facilities, as kidney function naturally diminishes with age. Nitrofurantoin may be used with caution for short-course treatment only in the presence of mild renal impairment (eGFR greater than 30 mL/min) when the benefits are expected to outweigh the risks. Patients with renal impairment (eGFR &lt;45 mL/min) should never however be placed on nitrofurantoin for long-term prophylaxis.</li> <li>There are <b>two nitrofurantoin formulations available: Nitrofurantoin immediate release capsules (MacroDantin®) and Nitrofurantoin prolonged release capsules (MacroBid®)</b>. For the treatment of infection the prolonged release capsules are dosed twice daily whilst the immediate-release capsules are dosed four times daily. These products are not interchangeable.</li> </ol>
<b>Trimethoprim</b>	<b>Green</b>	<p>Trimethoprim is another preferred option for the treatment of uncomplicated lower UTI. However, the rate of trimethoprim resistance in <i>E. coli</i> UTIs is increasing and exceeds 30% in some laboratory reports across Ireland. Empiric trimethoprim is increasingly only an option where risk of resistance is low (e.g. in a patient without a previous significant antibiotic exposure or urine culture has confirmed a trimethoprim-susceptible isolate). It has been recently removed from empiric guidelines for treatment of UTI in residential care facilities due to the risk of resistance in this population.</p>
<b>Cefalexin</b>	<b>Green</b>	<p>Cefalexin is the narrowest spectrum cephalosporin available orally (1st generation) and is an option for treatment of UTIs (both lower and upper). It is broader than nitrofurantoin or trimethoprim and reaches systemic levels and therefore should generally be avoided in uncomplicated UTI, unless there is no suitable alternative, to prevent the emergence of resistant organisms and <i>C. difficile</i> infection.</p>
<b>Fosfomycin</b>	<b>Green</b>	<p>Fosfomycin, a narrow spectrum agent, is suggested for use as a second-line agent only. Some multi-drug resistant UTI isolates (including ESBL-producing <i>E.coli</i> and CPE) are susceptible to fosfomycin, which is also available as an injection for severe infection with proven susceptibility. To preserve the usefulness of this drug, its use should be limited where possible to treatment of multi-drug resistant organisms only. Fosfomycin is not recommended in patients with creatinine clearance &lt;10 mL/min. Fosfomycin is not licenced for the treatment of UTI in men.</p>
<b>Amoxicillin</b>	<b>Green</b>	<p><b>Amoxicillin</b> is <b>not</b> recommended as empiric therapy for UTIs, as resistance rates of approximately 60% amongst <i>E. coli</i> isolates have been described in recent Irish studies. It should therefore only be prescribed where cultures have been taken and amoxicillin susceptibility has been confirmed.</p>
<b>Co-amoxiclav</b>	<b>Red</b>	<p><b>Co-amoxiclav</b> is a very broad spectrum agent and as such is not a preferred treatment option for UTIs in the community unless no safer, narrower spectrum alternative is available; particularly in uncomplicated cystitis if a locally acting agent such as nitrofurantoin could be used, or in complicated UTI if a narrower spectrum agent such as cefalexin could be used. Resistance to co-amoxiclav is increasing in Ireland, and its use is considered one of the drivers of ESBL producers.</p>
<b>Ciprofloxacin</b>	<b>Red</b>	<p>Ciprofloxacin is a very broad-spectrum agent, heavily associated with <i>C. difficile</i> infection and multiple rare but serious long-lasting adverse effects (see 'Fluoroquinolone Warnings 2019 Update' under 'Safe Prescribing' on <a href="http://www.antibioticprescribing.ie">www.antibioticprescribing.ie</a>). It is not recommended for the empiric treatment of UTI. It may be considered for targeted therapy of multi-drug resistant infections, where there are no other appropriate options and cultures have shown sensitivity. Patients should be informed of the risks associated with ciprofloxacin prior to initiating treatment.</p>

## UTI Prophylaxis and De-prescribing

Specialist opinion should be considered for patients with recurrent UTI. In particular, it is advisable to refer men, pregnant women and children under 16 for specialist opinion.

### ■ Definition of recurrent UTI.

Recurrent UTI in adults is defined as two or more UTIs in the last six months or three or more UTIs in the last 12 months.

### ■ Persistent asymptomatic bacteriuria (ASB) is NOT the same as recurrent UTI

- Urinary growth of bacteria in an asymptomatic individual (asymptomatic bacteriuria) is common, particularly in older people. It does NOT require treatment in most cases, except in pregnant women and prior to urological procedures which breach the mucosa.

### ■ Recurrent or persistent lower urinary tract symptoms are not always due to recurrent UTI.

Many conditions can cause similar symptoms, consider:

- Sexually transmitted infections;
- Postmenopausal atrophic vaginitis;
- Vulvovaginal candidiasis;
- Vulval lichen sclerosis, psoriasis or other dermatological conditions;
- Vulvodynia.

## Treatment

### ■ Non-antimicrobial measures

- In non-pregnant females with recurrent lower UTI, non-antimicrobial measures should be maximised prior to consideration of antimicrobial prophylaxis

- Give advice on **behavioural measures** which may reduce the risk of recurrent UTI. Note that there is limited evidence for these interventions but, anecdotally, many patients find them effective.

- Increase fluid intake
- Vulval care: Avoid use of potential irritants such as soaps, perfumes, talcs, cleansing wipes, disinfectants etc. Do not wash too often (once a day is usually sufficient). Use an emollient-based product or plain warm water to wash. Consider a barrier cream or ointment in incontinence.
- Advise post-coital voiding
- Do not habitually delay urination
- Avoid constipation
- Wipe from front to back after defecation

### ■ Consider **vaginal oestrogens** in post-menopausal women

- There is evidence that **D-mannose** (2g daily) is effective in reducing the risk of recurrent UTI in non-pregnant female patients, however it is based on one small RCT. Non-pregnant women may wish to try D-mannose, as a self-care treatment. The sugar content should be considered.

- There is currently little or no evidence of efficacy of **cranberry or alkalinising products** in the treatment of lower urinary tract infections. However, some patients with recurrent UTI may wish to try cranberry products to prevent UTI. The benefit of their use is uncertain but there is low quality evidence showing some benefit

for reducing the risk of UTIs, specifically in non-pregnant women, and children and young people. Pregnant patients, men and children should seek specialist advice however before taking. Advise patients to be aware of the sugar content of such products.

### ■ Antimicrobial Prophylaxis

- If a patient suffers from UTIs of such frequency and severity that it chronically affects their wellbeing, antimicrobial prophylaxis, either **single-dose** (e.g. post-coital) or **continuous**, can be considered if non-antimicrobial measures are unsuccessful. However, the side-effects and consequences of antibiotic prophylaxis should be carefully considered:

- All antibiotics are associated with a risk of adverse effects such as *C. difficile* infection, thrush, GI disturbances & skin reactions (cefalexin & trimethoprim)
- Long-term nitrofurantoin use is associated with multiple adverse effects, including liver damage, pulmonary fibrosis and peripheral neuropathy. Treatment should be withdrawn and it should be reported to the HPRA if any of these emerge.
- Continuous antimicrobial prophylaxis is strongly associated with development of antimicrobial resistance. There is the risk that the prophylactic agent will be lost as a future treatment option.

- When a trial of antimicrobial prophylaxis is given, **the patient should be advised** regarding:

- The fixed nature of UTI prophylaxis for 3-6 months, not longer. Documenting and triggering a review date in the patient's record, and on the repeat prescription, is strongly advised to avoid prolonged courses of antibiotics without review
- The risk of resistance developing with long term antibiotics
- The possible adverse effects of long term antibiotics
- The need to seek medical help if symptoms of an upper UTI develop

- In patients with an **identifiable trigger** (eg sexual intercourse), single-dose prophylaxis (e.g. post-coital) is preferred as it is as effective as continuous prophylaxis in preventing recurrent UTI, but minimises antibiotic exposure and associated adverse effects and development of resistance.

- It may be appropriate to use "**standby antibiotics**" as a preferred antimicrobial strategy in selected patients as there is evidence that self-diagnosis of cystitis has a high positive predictive value and the rationale for this approach is to facilitate early treatment.

## Deprescribing UTI prophylaxis:

- **Review antimicrobial prophylaxis at 3 - 6 months**, with a view to stopping. There is no evidence of any additional benefit from such prophylaxis

beyond 3-6 months. There is significant evidence of harm. After a 3 - 6 month period of antibiotic prophylaxis, many patients can stop without a return of symptoms.

- Patients who have breakthrough infections should have urine cultures taken and a clinical review to discuss ongoing management and/or need for referral.
- For further advice on deprescribing UTI prophylaxis, see [www.antibioticprescribing.ie](http://www.antibioticprescribing.ie)

### Self-care advice for the treatment/prevention of UTIs

- Paracetamol and ibuprofen (if no contraindications) are suitable pain relief options for patients with UTI and if mild cystitis/uncomplicated lower UTI, pain relief on its own may be sufficient to treat the UTI. A hot water bottle can also help.
- Patients should be advised to drink plenty of water to avoid dehydration and increase the flushing action through the urinary tract to eradicate bacteria.

- Evidence supporting the use of probiotics to prevent recurrent UTIs is currently inconclusive.

- Sexual intercourse should be avoided during cystitis as it may make symptoms worse.

- Patients should be advised on avoiding triggers and lifestyle changes if frequent cystitis is an issue. These include:

- Not using perfumed bubble bath/ bath bombs/ soaps around the genital area;
- Showering rather than bathing can reduce contact time with irritating soaps;
- Emptying your bladder fully (double-void) and as soon as you feel the urge to;
- Staying hydrated;
- Always wiping from front to back when you go to the toilet;
- Emptying your bladder after intercourse;
- Wearing breathable cotton underwear and not wearing jeans/ trousers too tight;
- Avoiding diaphragms as a means of contraceptive if relevant.

## Catheterised Patients and Patients in Residential Care Facilities

### Catheterised patients

- A catheter-associated UTI (CA-UTI) refers to UTIs in someone who is catheterised or who had a catheter in place within the past 48 hours.
- A catheter makes it easier for bacteria to enter the urinary tract (it provides a ladder to the bladder) and cause infection.
- Antibiotic prophylaxis is generally not appropriate for the prevention of UTI in catheterised patients because of its limited benefit and the risk of antibiotic-associated harm to the patient.
- Antibiotic prophylaxis is not appropriate for urinary catheter changes unless there is a definite history of UTIs due to catheter change.
- Due to the high incidence of asymptomatic bacteriuria in patients of any age with a catheter, the use of dipstick urinalysis is not routinely recommended in this cohort. This applies to persons in the community, hospital and residents in long-term care facilities.
- The best way to prevent CA-UTI is to use catheters as little as possible and for as short a time frame as possible.

### Patients in Residential Care Facilities

- UTI is the most common type of infection encountered in residential care settings.
- Due to the high incidence of ASB in persons over 65 years of age, the use of dipstick urinalysis is not a useful guide to assessment of UTI and is not recommended in this group. This applies to persons in the community, hospital and residents in long-term care facilities.
- A point prevalence survey carried out in 86 HSE Older Persons Residential Care Facilities in 2020 found that urinary tract infections accounted for 51% of therapeutic antimicrobials prescribed and 86% of prophylaxis. Over 60% of patients on UTI prophylaxis had been on the treatment for over 12 months. It is recommended that UTI prophylaxis be reviewed every 3-6 months with a view to stopping. Community pharmacists can greatly impact this through intervening during medication use reviews (MURs) in long term care facilities they dispense and supply to.
- Approximately 50% of residents were found to have some degree of renal impairment. This can have a major impact on drug metabolism, in particular, nitrofurantoin as outlined above.

To support antimicrobial stewardship in the community, each Community Health Organisation has an antimicrobial pharmacist. Contact details can be found on <https://www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/about-us/>

References available on request

Figure 2: It is important to drink plenty of water during a UTI and to prevent UTIs



# CPD overview

## Self-appraisal

- What do you know about management and treatment of UTIs?
- Am I aware of the antibiotics used in the treatment of UTIs?
- Can I offer self-care advice for the treatment/prevention of UTIs?

## Personal plan

Including a list of desired learning outcomes in a personal learning plan is a helpful self-analytical tool.

- Create a list of desired learning outcomes.
- How will I accomplish these learning outcomes?
- Identify resources available to achieve learning outcomes.
- Develop a realistic timeframe for the plan.

## Action

Activities chosen should be outcomes based to meet learning objectives.

- Implement plan.
- Read this article on An Update on UTI Management for Community Pharmacists.
- Evaluate professional resource materials available in the pharmacy and source additional material if necessary.
- Evaluate patient support material and source additional material if necessary.

## Evaluate

Consider outcomes of learning and impact of learning.

- Have I met my desired learning outcomes?
- Do I now feel confident to engage with prescribers and patients on UTI Management?
- Provide an example(s) of changes that I have implemented in my pharmacy practice.
- Have further learning needs been identified?

## Document your learning

- Create a record in my ePortfolio.
- As part of this record, complete an evaluation, noting whether learning outcomes were achieved and identifying any future learning needs.

## Your 5-minute assessment



Answer the following five questions:

1. Which of the following drugs should not be used to treat a UTI in patients with severe renal impairment?
  - a) Amoxicillin
  - b) Trimethoprim
  - c) Nitrofurantoin
- 2) Which of the following drugs is not currently recommended for empiric treatment of UTI in Ireland due to high resistance rates?
  - a) Nitrofurantoin
  - b) Cefalexin
  - c) Amoxicillin
- 3) True or False? Ciprofloxacin is a broad spectrum agent associated with *C. diff* and is not recommended for empiric treatment of uncomplicated cystitis.
- 4) True or False? A recurrent UTI can be defined as 1 or more UTIs in 6 months or 2 or more in one year.
- 5) Which of the following statements is TRUE?
  - a) Antimicrobial prophylaxis for UTI should be reviewed after 12 months with a view to stopping.
  - b) Ibuprofen is not a suitable pain reliever for a cystitis patient.
  - c) Catheterised patients are not at greater risk of UTI.
  - d) Dipstick urinalysis is not routinely recommended in patients over the age of 65 or those with a catheter due to high incidence of asymptomatic bacteriuria in these patients.

Answers  
1. C. 2. C. 3. True. 4. False. 5. D