NHS
North East and North Cumbria

Management of Symptomatic Recurrent Uncomplicated Urinary Tract Infections in Adult Women

Introduction

This document gives guidance on the management of adult women patients with recurrent urinary tract infections (RUTI). This guideline is intended for non-pregnant, non-catheterised and aged 16 years and over.

RUTI is defined as[1]:

- Three or more episodes of lower urinary tract infections in the last 12 months;

Or

- Two or more episodes of lower urinary tract infection in the last 6 months.

RUTI includes lower UTI and upper UTI (acute pyelonephritis) and may be due to relapse (with the same strain of organism) or reinfection (with a different strain or species of organism) and is particularly common in women.

A baseline history at the outset is helpful to understand the impact on the patient, which treatment strategies may be successful, and monitor effectiveness of chosen treatments. Using a shared decision making approach can help to establish the person's existing beliefs and preferences around RUTI and management options. Changes in the evidence base and guidelines in recent years may mean these differ from current recommendations and require further discussion.

This guidance provides information on evidence-based strategies to consider and if these are unsuccessful, guidance on which antibiotics are required and recommendations on choice, dose and duration. This includes;

- Self-care
- Non-antimicrobial therapies
- Trigger antibiotics
- Short term treatment
- Long term prophylaxis

Referral for recurrent UTI's

Referral or seeking specialist advice from the most appropriate specialty on further investigation and management is recommended for[1,2]:

- People with recurrent upper UTI
- People with recurrent lower UTI when the underlying cause is unknown
- People with recurrent lower UTI due to relapse
- Pregnant women.
- People with suspected cancer in line with the NICE guideline on suspected cancer: recognition and referral

Developed by	NENC AMS Subgroup of NENC AMR and HCAI Board
Approved by	APC
Version	1.1
Approved	Jan-23
Review	Jan-26

- People who are catheterised, so as to ensure appropriate catheter care and reduce the risk of infection (more than two episodes within 12 months).
- People who do not respond to prophylactic antibiotics, including two or more episodes of UTIs returning after stopping prophylactic antibiotics.
- People with structural abnormalities e.g. renal stones.
- People with neurological disease e.g. spinal cord injuries.

Self-care

Explore with patients with recurrent UTI the behavioural and personal hygiene measures and self-care treatments that help to reduce the risk of UTI[1,2]. Select the appropriate advice for your patient depending on co-morbidities:

- Drinking enough fluids to avoid dehydration, especially during hot weather
- Not delaying habitual and post-coital urination
- Wiping from front to back after defaecation
- Not douching or wearing occlusive underwear.
- Consider alternative to spermicide-containing contraceptives as these can increase the risk of UTIs[3].

Non-antimicrobial therapies

Vaginal (not oral) oestrogen:

Consider the lowest effective dose of vaginal oestrogen for postmenopausal women if behavioural and personal hygiene measures alone are not effective or appropriate, as they can reduce the risk of UTI[1,2].

Discuss the following with the woman to ensure shared decision-making:

- The severity and frequency of previous symptoms
- The risk of developing complications from recurrent UTIs
- The possible benefits of treatment, including for other related symptoms, such as vaginal dryness
- The possible adverse effects such as breast tenderness and vaginal bleeding (which should be reported because it may require investigation)
- The uncertainty of endometrial safety with long-term or repeated use
- Preferences of the woman for treatment with vaginal oestrogen.

Review treatment within 12 months, or earlier if agreed with the woman[2].

Vaginal oestrogen products are not licensed for preventing recurrent UTI, so this use would be off-label. Do not offer oral oestrogens (hormone replacement therapy) specifically to reduce the risk of recurrent UTI in postmenopausal women[2].

Methenamine hippurate[2,4,9]:

- Recent trial data has shown non-inferiority of methenamine when compared to antibiotic prophylaxis[9].
- Consider use of methenamine as an antibiotic sparing treatment
- Review ongoing therapy after six months.
- BNF lists methenamine as a medication less suitable for prescribing, although they acknowledge that it may have a role in the prophylaxis and treatment of chronic or recurrent uncomplicated lower UTIs[5].

Over the counter, purchasable options (not available on prescription):

- Some women with recurrent UTI may wish to try D-mannose if they are not pregnant[1,2].
- Some women with recurrent UTI may wish to try cranberry products if they are not pregnant (evidence of benefit is uncertain and there is no evidence of benefit for older women)[1,2].
    - Patients taking warfarin should be advised to avoid cranberry products due to potential interactions[5].
- Be aware that evidence is inconclusive about whether probiotics (lactobacillus) reduce the risk of UTI in people with recurrent UTI[2].

Assessment

- Arrange urine culture to check for resistant organisms.
- If appropriate, exclude chlamydia
- Consider referral to urology/urogynaecologist, if recurrent UTI in women with history of:
    - Pelvic cancer or pelvic radiotherapy
    - Complex pelvic surgery
    - Urinary incontinence or prolapse procedures with surgical mesh.

Take a careful history to distinguish between

- Relapsing UTI – typically the same organism identified on culture with small gaps between treatment and without intervening negative urine cultures.
- Recurrent UTI – different organisms or resolution of symptoms and significant gaps between episodes

Relapsing UTI

Suggests a persistent infective source such as a focus of infection e.g. stone, anatomical anomaly or abscess. Unlikely to improve unless focus is addressed. All patients with relapsing infection should be referred to a urologist.

Recurrent infection

Take a careful history to look for trigger factors (see below) for UTI. If a trigger factor is found, consider steps to reduce the risk from the trigger factor and/or consider single dose prophylaxis given at the time of the trigger factor (e.g. sexual intercourse).

If this does not help, recurrent UTIs should be treated with provision of rescue antibiotic treatment in preference to long-term prophylaxis whenever possible (see below).

If no other strategy works, and a 3–6 month trial of daily prophylaxis is deemed appropriate, then choose the most appropriate antibiotic based on culture and sensitivity and patient characteristics. Explore the patient's expectations of treatment success, duration, monitoring, review and deprescribing.

Stop after six months and monitor for any recurrence.

Trigger factors

Prescribe antibiotics and advise that a single dose is to be taken when exposed to a trigger. Triggers may include:

- intercourse
- menstruation
- constipation

Note: Post-coital antibiotic prophylaxis should be taken within two hours of coitus.

Other triggers may include menopause and diabetes (new or poorly controlled). Consider treating underlying issues before starting antibiotics.

Treatment choice must be made with consideration of recent culture and sensitivity results if available.

First choices[2]:

- Nitrofurantoin 100mg single dose when exposed to a trigger

OR

- Trimethoprim 200mg single dose when exposed to a trigger.

Second choice[2]:

- Amoxicillin 500mg single dose when exposed to a trigger

OR

- Cefalexin 500mg single dose when exposed to a trigger.

The patient should be counselled on possible adverse effects of antibiotics, particularly diarrhoea and nausea and advised to return for review within 6 months. If there are symptoms of a UTI despite taking prophylaxis then the patient should seek medical help[2]

Rescue antibiotics

Choice of antibiotic should be made with consideration of recent (within the last 3 months) culture and sensitivity results if available or in line with NICE guidance (NG109) Urinary tract infection (lower)

Issue as an acute prescription and frequent requests should trigger a clinical review. If there are any trigger factors for UTI, take steps to reduce risks and manage underlying conditions before starting antibiotics (as above).

Rescue antibiotics should be taken at the first sign of urinary tract infection. This strategy is likely to be effective in patients that have clear symptomatology. Provide patient with urine sample pot to collect a sample prior to initiation of antibiotics.

Antibiotic prophylaxis course

An antibiotic prophylaxis course should only be used in patients with either a temporary reason for requiring extended prophylaxis or in cases where alternative strategies have failed and the risk of infection is deemed to clearly outweigh the risk of development of antimicrobial resistance.

When prescribing prophylactic antibiotics, factors that should be considered include:

- risk profile of antibiotic
- microbiology results
- suitability of antibiotic (allergy, renal function, other comorbidity or risk factors)

Cycling of antibiotics is not encouraged. It is common for patients receiving UTI prophylaxis to subsequently become colonised with bacteria that are resistant to the antibiotic being given and develop infections with resistant bacteria. The act of cycling antibiotics during prophylaxis will tend to result in colonisation with multi-drug resistant bacteria.

Before deciding to commence antibiotic prophylaxis, use a shared decision making approach to explore the following with the patient:

- Antibiotic prophylaxis is usually short in duration (3-6 months) and there is no evidence of additional benefit beyond 6-12 months
- There is a risk that long term antibiotics may make any future acute UTIs more difficult to treat due to resistance
- It is good practice to write a clear end date on the antibiotic prescription so that it is clear to patient, other colleagues and community pharmacy when the prophylactic course should end / be reviewed.

Set a review date for 3-6 months as agreed with the patient.

Treatment choice must be made with consideration of recent culture and sensitivity results if available.

First choices[2]:

- Nitrofurantoin 50mg at night

OR

- Trimethoprim 100mg at night

Second choices[2]:

- Amoxicillin 250mg at night

OR

- Cefalexin 125mg at night

Break through infections should be treated according to culture and sensitivity results, once the infection is resolved the original prophylaxis should be re-started

Reviewing and monitoring prophylaxis

Following initiation, the patient should be reviewed for a clinical response after three months and after stopping the antibiotics at six months. When reviewing antibiotic prophylaxis, confirm the effectiveness of the strategy (is the frequency of UTI significantly lower when on prophylaxis) and check for the development of resistance.

Development of a single UTI with a resistant bacteria is not necessarily an indication to change the prophylaxis as a change is likely to only result in further resistance. The measure of success of any prophylaxis, regardless of the presence of resistant bacteria, is whether or not it reduces the frequency of UTI.

After six months of prophylaxis is complete, discuss behavioural and personal hygiene measures and self-care with the patient, and discuss alternative strategies for management and prevention.

No break-through UTIs in last six months

- Stop prophylaxis or offer standby antibiotics if patient concerned – explore simple self-care measures with the patient.
- Monitor for any recurrences.

Two or more break-through UTIs (in last six months) or urine culture resistant to prophylactic agent

- Consider alternative strategies for management/prevention and stop prophylactic antibiotic.
- Consider referral.

Monitoring for adverse effects

Please refer to the BNF[5] and the Summaries of Product Characteristics (SPCs)[6,7] for full prescribing details and monitoring information.

Nitrofurantoin[5,6,8]

Nitrofurantoin is the first line choice as it generally has a lower level of resistance compared with other antibiotic choices, however there are also risks associated with prescribing that clinicians and patients must be aware of before commencing a course, particularly longer courses for prophylaxis.

Tests prior to starting

- Full Blood Count
- Liver Function Tests
- Renal Function - urea and electrolytes, creatinine, avoid if eGFR less than 45ml/min. However, a short course (3-7 days) may be used with caution if eGFR 30-44ml/min

Tests during treatment

- Liver Function Tests every 3-6 months (due to a risk of cholestatic jaundice and hepatitis)
- Renal Function every 3-6 months - urea and electrolytes, creatinine.

Hepatotoxicity

The onset of hepatotoxicity can be insidious and symptoms can be non-specific (e.g. nausea, rash, headache, flu-like symptoms). Cholestatic jaundice is generally associated with short-term therapy (usually up to two weeks) whereas chronic active hepatitis, occasionally leading to hepatic necrosis, is generally associated with long-term therapy (usually after six months).

Pulmonary

Nitrofurantoin can cause drug induced pulmonary disease/toxicity, which can potentially be serious and even fatal. The severity of chronic pulmonary reactions and their degree of resolution appear to be related to the duration of therapy after the first clinical signs appear

and elderly patients should be monitored closely. It is therefore important to recognise symptoms as early as possible. Pulmonary toxicity can be either acute or chronic.

- Acute pulmonary reactions usually occur within the first week of treatment and are reversible when treatment is stopped. Acute symptoms include: fever, chills, cough, chest pain, breathlessness, and chest x-ray abnormalities[6]
- Chronic interstitial fibrosis may occur after six months of treatment. Symptoms are dyspnoea, non-productive cough. There is a good prognosis if nitrofurantoin is discontinued promptly.

Patients should also be advised to report any symptoms suggestive of pulmonary toxicity, such as cough, chest pain and shortness of breath as soon as possible to a healthcare professional.

British National Formulary (BNF) advice is to discontinue if there is a deterioration in lung function for patients on long-term therapy[5].

Nitrofurantoin must be withdrawn at the first sign of pulmonary damage

Neurological
Peripheral neuropathy is seen with long-term therapy and associated with renal failure not necessarily severe enough to raise blood urea. Symptoms are paraesthesia beginning in extremities, ascending bilaterally and symmetrically followed by paralysis of varying extent. In most patients, it occurs within 45 days of starting and patients should be advised to report paraethesia[5,6].

Trimethoprim[8,7]

Tests prior to starting
- Full Blood Count
- Renal Function (urea, electrolytes and creatinine). Adjust dose according to renal function.

Tests during long-term treatment
- Full Blood Count - every six months (see below)
- Renal Function (urea, electrolytes & creatinine) - every six months.

Contraindication
- Do not prescribe if patient is on methotrexate

Clinical monitoring during treatment

Folate deficiency
There is a theoretical risk of folate deficiency with long-term use of trimethoprim. Caution should be exercised in patients with a predisposition to folate deficiency (e.g. elderly patients) and adding a folate supplement should be considered. The manufacturer recommends blood counts on long-term therapy[7], but evidence of practical value is unsatisfactory. Megaloblastic anaemia has been reported but is rare and usually mild, except in pre-existing folate deficiency[13].

Blood disorders
Patients and their carers should be told how to recognise signs of blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop. Manufacturer recommends monitoring full blood counts[13].

Hyperkalaemia
Close monitoring of serum electrolytes is advised in patients at risk for hyperkalaemia. Hyperkalaemia is a very common adverse effect of trimethoprim treatment[13]

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