Guidelines for the Primary Care Management of Recurrent Urinary Tract Infections in Adults

Definition of recurrent lower urinary tract infection:

The symptoms of a lower urinary tract infection include: frequency, dysuria, urgency and suprapubic pain. Recurrent lower urinary tract infection (rUTI) is defined as:

2 or more episodes of lower urinary tract infection in the last 6 months, OR
3 or more episodes of lower urinary tract infection in the last 12 months.

Recurrent lower urinary tract infection (rUTI) does not include asymptomatic bacteriuria, which refers to the presence of bacteria in the urine without any accompanying symptoms, or in catheterised patients. Asymptomatic bacteriuria should not be screened for or treated, unless prior to urological surgery or in pregnancy (positive cultures in pregnancy should be confirmed with a second culture confirming the same organism prior to treating).

Consider whether referral is required for patient with recurrent UTIs:

Consider referring the patient to a specialist based on the following factors:

1.1 Red Flags for Referral to Urology:

- Adults aged 45 years and over with visible (frank) haematuria, where the haematuria is unexplained in the absence of UTI, or persists or recurs following successful treatment of a suspected or confirmed UTI. Referral should be made via the suspected cancer (2-week-wait) pathway.
- Neurological disease e.g., spinal cord injury, spina bifida.
- Prior abdominopelvic malignancy.
- Pneumaturia or faecaluria.
- Proteus on repeat urine cultures.
- Suspected stone.
- All recurrent UTIs in pregnancy should be discussed with the Obstetrics team
- Obstructive symptoms, known structural/functional abnormality (including previous urinary tract surgery pelvic organ prolapse surgery or trauma), OR any of the following features are present on renal ultrasound:
    - Hydroureter or hydronephrosis,
    - Bladder OR ureteric OR obstructive renal stones (for non-obstructive renal stones please use advice and guidance)
    - Post-micturition residual volume greater than 150ml

Consider risk factors:

A sexual history and investigations for sexually transmitted infections should be performed if appropriate. In peri- and post-menopausal women, trans men and non-binary people with a female urinary system atrophic vaginitis may cause urinary symptoms and may increase the risk of bacteriuria. Due to low oestrogen levels in post-menopausal women, trans men and non-binary people with a female urinary system, consider using intravaginal oestrogens for those with recurrent UTIs.

Based on "Guidelines for Recurrent Urinary Tract Infections in Adults" by Authors: Dr Amelia Joseph, Mr Richard Parkinson and Dr Jane Coleman GP. http://www.nottsapc.nhs.uk/media/1217/uti-prophylaxis-guideline.pdf

Microbiological confirmation:

Patients with rUTIs should have a mid-stream urine (MSU) sample sent for culture **prior** to antibiotics being initiated, in order to confirm infection and guide antibiotic therapy. Patients should be counselled on how to provide a specimen to minimise the chance of contamination. http://patient.info/health/midstream-specimen-of-urine-msu

Urine cultures sent in the absence of symptoms are unlikely to be helpful, may detect asymptomatic bacteriuria and lead to inappropriate antibiotic use. Antibiotic treatment of asymptomatic bacteriuria is more likely to be harmful than beneficial.

In symptomatic patients with pyuria and a negative culture who do not respond to antibiotics as expected, consider whether an alternative diagnosis may be relevant. Sterile pyuria can occur in a number of infective conditions, including sexually transmitted diseases (e.g., Chlamydia), infections with organisms that are difficult to grow on standard culture, and renal tuberculosis, as well as non-infectious causes.

It is important to note that a negative urine culture in symptomatic patients with pyuria does not rule out infection. Symptomatic patients with persistent sterile pyuria (persistent presence of white blood cells in the urine that repeatedly do not grow any organisms on routine culture) and symptoms strongly suggestive of urinary tract infection should be discussed with the duty microbiologist.

Management of initial presentation of recurrent UTI in non-pregnant women, trans men and non-binary people with a female urinary system

The following conservative measures should be tried prior to antibiotic prophylaxis:

Self-care measures:

- Encourage better hydration if necessary and more frequent voiding if patient only visits the lavatory infrequently.
- Patients can be advised to try D-mannose and/or cranberry tablets (available without prescription), but there is very limited evidence of benefit.
- For sexually active women, trans men and non-binary people with a female urinary system:
    - Advise post-coital voiding
    - Avoid use of contraceptive diaphragm and spermicide
- Avoid using feminine hygiene products (e.g. cosmetic bath products or douches)
- Perineal hygiene – i.e. wiping front to back.
- Avoid using flannels. A clean non-scented disposable wipe is preferable.
- Offer TARGET - Treat Your Infection Urinary Tract infection Patient Information Leaflet

Vaginal oestrogens:

Current NICE guidelines state that vaginal oestrogens [unlicensed indication] can be used for women, and trans men and non-binary people with a female urinary system who are experiencing perimenopause or menopause, or who have already experienced menopause, with recurrent UTIs at the lowest effective dose if behavioural and personal hygiene measures alone are not effective or appropriate. The prescriber should follow relevant professional guidance, taking full responsibility for the decision.

Discuss the following with the patient 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 patient for treatment with vaginal oestrogen.

This is a highly preference-sensitive decision, involving a trade-off between benefits, risks and when appropriate, costs. Should vaginal oestrogens be considered, local experience and published evidence suggests using once each night for two weeks followed by twice-weekly applications for 4 weeks initially. Consideration should be given to continuing them for 6-12 months and then review treatment within 12 months, or earlier if agreed with the patient. Link for estriol 1mg/g vaginal cream (0.1% cream) 15g patient letter

Recurrent UTI Prophylaxis Prescribing Strategies

The relative risks and benefits of the following recurrent UTI prophylaxis prescribing strategies should be discussed with the patient. These strategies should be in addition to the conservative measures detailed above and are based on the patient's history and risk factors.

Standby antibiotics

- If the patient is able to wait, infection should first be confirmed by MSU prior to commencing standby antibiotics.
- Offer TARGET – Treat Your Infection Urinary Tract infection Patient Information Leaflet.



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- A patient advice sheet and boric acid container for pre-antibiotic MSU should be provided to the patient.
- A 'self-start' course of antibiotics, prescribing an agent according to previous known sensitivities and choosing the narrowest spectrum agent available.
- Provide safety-netting advice, including when to seek medical attention if they develop fever, loin pain, or symptoms are not improving by 48 hours.
- This option limits antibiotic exposure and risk of resistance emerging and may be the more suitable option for patients with <1 UTI per month.

Single-dose Antibiotic (one-off dose) / Post-coital antibiotics

- This can be considered for women, and trans men and non-binary people with a female urinary system, who are not pregnant for rUTIs due to an identifiable trigger.
- For rUTIs triggered by sexual intercourse, this strategy is as effective as continuous antibiotic prophylaxis and reduces antibiotic exposure and the risk of resistance emerging as well as adverse effects encountered.

Continuous Antibiotic Prophylaxis

- Continuous antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance.
- **A 6-month trial** of a low-dose nightly antibiotic may be beneficial if rUTIs are occurring ≥1 per month and are not triggered by sexual intercourse.
- Patients should be counselled at an early stage that antibiotic prophylaxis is not usually a lifelong treatment.
- **A review date must be clearly recorded in the patient's medical notes and on any repeat prescriptions to ensure timely reassessment**.
- **Reassessment must occur at least every six months** to avoid inappropriate long-term use.

Continuous Urinary Antiseptic Prophylaxis (Methenamine hippurate)

- Methenamine hippurate may be considered only after documented failure of an antibiotic prophylaxis regimen or when antibiotic prophylaxis is contraindicated, and acts as a urinary antiseptic by converting to formaldehyde in acidic urine, which is directly toxic to bacteria.

Methenamine hippurate should be initiated and continued only when all of the following local criteria are met (see below and responsibilities section):

- **Eligible patients:** Non-pregnant adults aged 18 or over (men, women, trans and non-binary people with male or female urinary systems), only after documented failure of at least one antibiotic prophylaxis regimen or where antibiotic prophylaxis is contraindicated
- **Excluded patients**: Children and those who are pregnant (due to limited evidence and safety concerns). Contraindications as outlined in SPC.
- **UTI history:** Two or more episodes of acute bacterial cystitis, associated symptoms within the last 6 months, or at least 3 episodes within the previous year.
- **Prior management:** Documented failure of at least one antibiotic prophylaxis regimen or antibiotic prophylaxis contraindicated or declined after informed discussion of risks and benefits
- **Organism exclusion:** Previous urine cultures must not show Proteus or Pseudomonas species.
- **Urinary tract assessment:** No structural abnormalities seen on imaging and no evidence of a neuropathic bladder. Patients must be able to empty their bladder effectively.
- **Renal function:** Baseline eGFR must be greater than 10 mL/min/1.73m².
- **Initiation and review:** Initiated by a secondary-care specialist following documented assessment. Treatment should usually continue for 3–6 months (to confirm efficacy and tolerability), followed by a trial withdrawal period as advised by the specialist. The specialist must document a review plan, communicate the intended stop date to the GP, and advise on next steps if recurrence occurs. Continuation beyond six months requires clear evidence of benefit and agreement from the initiating specialist.
- May be continued in primary care only if clinical benefit is documented at review, a clear trial withdrawal plan is in place, and the specialist has confirmed ongoing suitability.
- **Treatment failure:** Discontinue if two or more symptomatic UTIs occur during 6 month treatment, if there is no reduction in UTI frequency, or if resistance is confirmed on culture.
- **Counselling and information:** The specialist should provide baseline counselling covering expected benefits, common side-effects (for example, mild gastrointestinal discomfort or rash), and the plan for review and trial withdrawal. GPs and other prescribers should refer to the SPC for full details of cautions, contraindications, and interactions.
- **Immediate discontinuation:** Required if the patient develops severe dehydration, metabolic acidosis. Methenamine must not be co-administered with sulfonamide antibiotics due to the rist of crtystalluria.

These are primary care guidelines - Methenamine is for specialist initiation (AMBER INITIATION) and referral is required

Responsibilities (also see information above)

Specialist responsibilities:

- Confirm eligibility and ensure at least one prior antibiotic prophylaxis regimen has failed.
- Counsel the patient on the purpose of methenamine, possible adverse-effects, review plan, expected duration, and the plan for trial withdrawal after 6–12 months in line with the specialist review plan.
- Initiate and monitor for 3–6 months to confirm efficacy and tolerability; primary care may assume prescribing once efficacy and tolerability are documented.
- Provide written advice to the GP on clinical benefit, information provided to patient and ongoing treatment plan including dose, review timing, and management of trial withdrawal or relapse.

GP responsibilities:

- Continue prescribing only when advised in writing by the initiating specialist.
- Undertake trial withdrawal as advised by the specialist after 6-12 months. Treatment may usually be reinstated if symptomatic recurrences return following cessation.
- Ensure reviewed as requested by the specialist including efficacy and tolerance. Patients should usually be reviewed after 6 months of prophylactic methenamine and at least every 6 months thereafter, or earlier if

clinically indicated.

- Stop if treatment failure, development of contra-indications, intolerable side-effects or evidence of non-adherence.
- Patients not responding to prophylaxis, or presenting with haematuria, recurrent upper UTI, or suspected obstruction, should be referred to urology for further investigation.
- Liaise with the specialist as needed for review outcomes, relapse, or adverse effects.
- Refer to the Summary of Product Characteristics (SPC) for full prescribing information

Primary or secondary care clinician may reinstate methenamine only if symptomatic recurrences return following cessation, and if other management approaches have failed.

There is some evidence that methenamine works in an acidic urine environment. In the ALTAR study, the value of urinary acidification was not explored. Therefore, routine dipstick testing is currently not advised in this guideline until further evidence is available and urine acidification products (i.e vitamin C) are NOT recommended for NHS prescribing.

Choice of agents:

The choice of agent should be based on patient preference, consideration of the patient's comorbidities, renal function and any contra-indicating factors

Choice of antibiotic should be based on **confirmed culture and sensitivity results** (wherever possible), and consider the patient's co-morbidities, renal function and any contra-indicating factors. Trimethoprim and nitrofurantoin are licensed for the prophylaxis of rUTIs. Nitrofurantoin is the first line choice for antibiotic prophylaxis.

The risk of adverse effects (see box below), as well as common side-effects such as rashes, oral/vaginal thrush and gastro-intestinal upset, should be discussed with the patient. Nitrofurantoin induced lung toxicity appears to occur in less than 1 in 1000 exposures. The spectrum of **nitrofurantoin induced pulmonary toxicity** includes acute or chronic interstitial pneumonia, pulmonary haemorrhage, bronchoconstriction, anaphylaxis, and pleural effusion.

Acute pulmonary reactions are probably underestimated. The incidence has been estimated to be anywhere from 1 in 550 to 1 in 5400 individuals. Acute toxicity is nearly 10 times more common than chronic. Toxicity can occur at relatively small doses, and does not appear to be dose-related.

If there is resistance to trimethoprim and nitrofurantoin, other agents may be considered after discussion with urology, urogynaecology and/or microbiology. Broader spectrum agents such as cefalexin, ciprofloxacin and co-amoxiclav have a higher risk of C.difficile diarrhoea and should not be routinely used for prophylaxis. In addition MHRA have issued an alert restricting the use of fluoroquinolone antibiotics e.g. ciprofloxacin

Antibiotic	Dose	Cautions and monitoring requirements
Nitrofurantoin **First line**	100mg immediate release One dose post-coital (off label) Or 50mg to 100mg at night	• Renal impairment: avoid if eGFR <45 ml/min. Consider checking renal function prior to commencing continuous prophylaxis, especially in the elderly. • Avoid if G6PD deficiency. • Use with caution in anaemia, diabetes, vitamin B or folate deficiencies. • Monitor full blood count, renal function and liver function tests every 3-6 months • **Advise the patient on the risk of pulmonary and hepatic fibrosis, and the symptoms (such as chronic cough) to report if they develop during treatment. Reactions can develop acutely or insidiously**. **The incidence has been estimated to be anywhere from 1 in 550 to 1 in 5400 individuals.** • Advise the patient on the risk of peripheral and optic neuropathy, and the symptoms to report if they develop during treatment.
Trimethoprim	200mg One dose post-coital (off label) Or 100mg at night	• Hyperkalaemia: caution when prescribing with drugs such as spironolactone, ACE inhibitor or angiotensin-II inhibitors. • Renal Impairment: Avoid if eGFR <15ml/min. Discuss with renal physician if eGFR <30ml/min. May increase serum creatinine. • Patients should be counselled on the risk of blood disorders and advised to seek attention if fever, sore throat, purpura, mouth ulcers, bruising or bleeding occurs.
Amoxicillin	250mg at night 500 mg One dose post-coital	• Avoid if history of anaphylaxis, urticaria or rash immediately after previous penicillin administration

Cefalexin	125mg at night 500 mg One dose post-coital	• Contra-indicated in patients with cephalosporin hypersensitivity • Patients with a history of immediate hypersensitivity to penicillin and other beta-lactams should not receive a cephalosporin

NB: Choose antibiotics according to recent culture and susceptibility results where possible. Consideration must be given to causative organism and resistance reporting. Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) need to be reserved for second-choice treatment when narrow spectrum antibiotics are ineffective.

Antiseptic	**Dose**	**Cautions and monitoring requirements**
Methenamine **AMBER INITIATION** **Urine acidification products (i.e vitamin C) are NOT recommended for NHS co-prescribing with methenamine.**	1 g twice a day	• Check baseline renal function (U&Es and eGFR); avoid if eGFR <10 mL/min/1.73m². LFTs only if hepatic impairment suspected. • Not for the treatment of UTI. • Avoid in patients with a history of febrile UTI or previous urosepsis. • Contraindicated in patients with gout, metabolic acidosis, or severe dehydration. • Hepatic impairment: Avoid. • Not recommended for use in children, or during pregnancy. • Use in men should be restricted to specialist urological initiation due to limited trial data in this cohort. • Uncommonly can cause epigastric discomfort and skin reactions.

Managing a patient who has had a prolonged course of prophylactic antibiotics:

Identifying patients for review:

- Review antibiotic prophylaxis for recurrent UTI **at least every 6 months.**
- Patients who have urine cultures confirming resistance to the prophylactic agent they are on, should have their prophylaxis stopped (exposure to antibiotic without benefit) and a clinical review to discuss ongoing management and/ or need for referral.

Stopping continuous prophylaxis:

- The proportion of patients who will return to suffering rUTIs after stopping continuous prophylaxis may be around 50%.
- This means a significant number of patients are able to stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of resistance emerging and side-effects.
- One option is to provide 'standby' antibiotics when stopping continuous prophylaxis which may give sufficient reassurance to patients for a trial off antibiotics.
- Consider referring patients who relapse after stopping continuous prophylaxis, if not already been investigated.
- Longer term prophylaxis may be helpful in those patients whose UTIs are suppressed when on prophylaxis and recur when prophylaxis is discontinued.

Managing 'breakthrough' UTIs in patients on antibiotic prophylaxis:

- The first breakthrough infection should be treated according to culture and sensitivity results, with the original prophylaxis being re-started once the infection has resolved if the culture confirms it is still sensitive to the prophylactic agent.
- If the culture shows resistance to the prophylactic agent, or multiple breakthrough UTIs occur (≥2 UTIs in 6 months), prophylaxis has proved ineffective and should be stopped.
- Consider an alternative prophylactic agent based on identification and sensitivity of the organism
- In absence of sensitivity data liaise with consultant microbiologist from acute Trust
- Consider referral to Urology or Urogynaecology at this point if not already been investigated.

Recurrent UTIs associated with urinary catheters:

- Cloudy or offensive urine alone does not merit treatment or investigation for UTIs in patients with urinary catheters.
- Do not use dipsticks to diagnose UTIs in patients with urinary catheters as symptomatic UTIs cannot be differentiated from asymptomatic bacteriuria on the basis of dipstick urinalysis.
- Look for associated localising or systemic features including flank pain, and exclude other potential sources of infection in catheterised patients who present with fever.
- Antibiotic prophylaxis generally does not significantly reduce the incidence of symptomatic infection and increases the risk of antimicrobial resistance. It is therefore not usually recommended to reduce the frequency of UTIs in patients with urinary catheters.
- Seek explicit guidance from a microbiologist before commencing antibiotic prophylaxis in patients with a urinary catheter.
- Obtain a urine sample from the sampling port of the catheter using an aseptic technique (in line with the NICE guideline on healthcare-associated infection) and send for culture and susceptibility testing.
    - If the catheter has been changed, obtain the sample from the new catheter.
    - If the catheter has been removed obtain a midstream specimen of urine.

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Superseded version	1.1 Harmonised guidelines for primary care management of recurrent urinary tract infections (rUTI) in adults within Hertfordshire and West Essex ICS - Harmonisation of Hertfordshire Medicines Management Committee (HMMC) and West Essex Medicines Optimisation Programme Board (WEMOPB) recurrent urinary tract infections guidelines - Review date removed and replaced with standard statement. - Version control box added 2.1 Addition of methenamine