Guidelines for Recurrent Urinary Tract Infections in Adults

The definition of recurrent Urinary Tract Infections (rUTI) is **three or more episodes of microbiologically proven UTI in 12 months or two or more in 6 months**.

Recurrent infections may be due to re-infection (a prolonged interval between infections) or bacterial persistence (frequent relapsing infections within short interval by the same organism). They should be diagnosed in line with the BNSSG UTI guidelines and a urine sample taken. It does not include episodes of bacteriuria without UTI symptoms (asymptomatic bacteriuria).

Red flags and other criteria for referral to urology

- All men– unless previously investigated by urology.
- Neurological disease where you suspect urinary tract infection may have neurogenic cause.
- In pregnancy – all recurrent UTIs should be discussed with the obstetrics team.
- Frank haematuria
- Pneumaturia or faecaluria
- Proteus on repeat urine cultures (often linked with stone disease)
- Suspected stone
- Obstructive symptoms or structural/functional abnormality causing >200ml residual urine on bladder scan. Consider Urology Advice and Guidance for women with residuals <200mls where GP is concerned this may be a causative factor for recurrent UTIs.

If a patient has any red flags refer for cystoscopy: persistent dysuria or storage problems despite antibiotic therapy, persistent non-visual haematuria despite treatment and significant smoking history.
Consider 2WW referrals: Suspected cancer: recognition and referral (nice.org.uk) remedy pathway and non-urgent referral in people aged 60 and over with recurrent or persistent unexplained urinary tract infections. If in any doubt, it is safer to ask for Urology Advice and Guidance or refer for cystoscopy.

First Line – Simple measures to limit UTIs

- Hydration (1.5-2L/day is recommended increasing with exercise or hot weather.)
- Treat constipation – this is a common factor in recurrent UTIs in the elderly and should always be assessed and treated.
- Advise to avoid delaying voiding once urge to void is present.
- Pre and postcoital voiding and advise that diaphragm and spermicide use are risk factors for UTI.
- Encourage relaxation of pelvic floor during voiding to ensure full bladder emptying.
- Hygiene measures e.g. wiping front to back, using water to wash after voiding, having showers rather than baths. Avoid flannels and scented washes/wipes.
- Consider D-mannose 2 grams daily. Self-care – can be purchased from health food stores or online.
- Consider cranberry tablets (avoid if on Warfarin) – these work for some women but good evidence is lacking. Two cranberry tablets a day. There is no evidence juice is effective. Self-care.

Ensure the Target Urinary Tract Infection information leaflet is given (there are separate leaflets for women under 65 years and older adults)

If fails to improve symptoms

1. UTIs should be diagnosed and treated in line with the UTI treatment guidelines during an acute UTI episode. (An MSU should be sent to establish sensitivities but a negative culture especially in the presence of pyuria does not rule out UTI in a symptomatic patient.)
2. Consider vaginal oestrogens for all peri/ post-menopausal women with recurrent UTIs. These should be trialled for 3-6 months and can safely be continued long term if beneficial. Estriol cream 0.1% and Estradiol vaginal tablets 10micrograms are on formulary. These can be added alongside systemic HRT which does not protect against UTIs.
3. All patients with recurrent UTI should be referred for a renal tract ultrasound (to detect stones, cysts, tumours, and other abnormalities) specifically requesting a post-void bladder residual volume (to detect voiding dysfunction) as part of this scan. In the presence of a normal ultrasound of the urinary tract and in the absence of non-visible haematuria (outsides of periods of symptomatic infection) a cystoscopy is often not necessary as the diagnostic yield is very low.

Second line – Single Dose Trigger Antibiotics or Standby Antibiotics

Single dose Trigger Antibiotics are taken when exposed to a known trigger (e.g. sexual intercourse / exercise). For rUTIs with a known trigger a single dose antibiotic strategy is as effective as continuous antibiotic prophylaxis, whilst reducing antibiotic exposure and therefore risk of resistance.

The choice of treatment should be based on recent sensitivities and examples are Nitrofurantoin 100mg or Trimethoprim 200mg stat taken when exposed to the trigger.

Standby antibiotics are a course of antibiotic which can be initiated when symptoms start. A urine sample should be obtained when the patient becomes symptomatic (provide specimen pot) but the patient can initiate antibiotics. Ensure the Target Urinary Tract Infection information leaflet is given as this has details of possible urinary symptoms and safety net to seek medical attention if develop fever, loin pain or symptoms not improving by 48 hours.

The choice of treatment should be based on previously known sensitivities and the BNSSG Lower UTI guideline.

Review at 6 months

Third line – Continuous Urinary Antiseptic or Antibiotic Prophylaxis

Continuous Urinary Antiseptic – **Methenamine Hippurate** is converted to formalderhyde in an acidic urine environment which is directly toxic to bacteria. It has been shown to be non-inferior to antibiotic prophylaxis for reducing the incidence of symptomatic UTIs over a 12-month process. Its use avoids the creation of antibiotic resistance and side effects. It can be initiated in women without urinary tract abnormalities or neuropathic bladder.

Continuous Antibiotic Prophylaxis is strongly associated with the development of antimicrobial resistance. Antibiotic choice should ideally be based on previous urinary cultures and sensitivities. Options include **Nitrofurantoin** (see cautions bellow) and **Trimethoprim**.

The patient should be counselled that prophylaxis is not usually a lifelong treatment. Treatment is given in this way to allow a period of bladder healing which makes UTIs much less likely. There is no evidence they have any additional benefit beyond 3-6 months treatment; therefore the treatment should ideally be discontinued after 6 months.

On prescribing, a review date of 3-6 months should be documented in the medical notes and on the prescription. The patient should be reviewed with a view to stopping the treatment as this time.

Drug	Dose	Cautions and Monitoring
Methenamine Hippurate (prescribe as Hiprex)	1 gram twice a day	Not for the treatment of UTIs Avoid in patients with a history of febrile UTI or previous urosepsis Renal impairment: avoid if GFR <10ml/min Hepatic impairment: avoid Contra-indications: gout, metabolic acidosis, severe dehydration Pregnancy: preferable to avoid as inadequate evidence of safety Side effects: uncommonly can cause epigastric discomfort and skin reactions
Trimethoprim	100mg nightly or 200mg one dose post trigger (off-label)	Monitoring of renal function and serum electrolytes should be considered with longer term use especially those at risk of hyperkalaemia. Regular haematological tests should be performed during long term therapy.
Nitrofurantoin	100mg nightly or 100mg immediate release one dose post trigger (off label)	Avoid if renal function GFR<45ml/min Long term Nitrofurantoin increases the risk of pulmonary toxicity and hepatic toxicity. If receiving long term, liver function and lung-function should be monitored. See last page for monitoring requirements on initiation and longer term. Patients should be counselled on the potential for pulmonary and hepatotoxicity associated with long term nitrofurantoin and consent to proceed with treatment documented. They should be advised to stop antibiotic immediately and arrange a review should they develop any symptoms of these including breathlessness / an increase in breathlessness on exertion; cough; yellowing of eyes/skin; unexplained bruising/bleeding; excessive itching.

Managing 'breakthrough' UTIs on a continuous prophylactic agent

Antibiotic prophylaxis

- The first breakthrough infection should be treated according to culture and sensitivity results if available, with the original prophylaxis held and then restarted once the infection has resolved if the culture confirms susceptibility 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 therefore proved ineffective and should be stopped or changed to an alternative prophylactic agent (antibiotic or methenamine).
- Consider referral to Urology at this point if not already referred.

Methenamine prophylaxis

- The breakthrough infection should be treated according to culture and sensitivity results if available.
- Methenamine prophylaxis should be continued alongside and after the antibiotic course for the breakthrough infection if there has been a good response.
- If multiple breakthrough UTIs occur (≥2 UTIs in 6 months), prophylaxis has therefore proved ineffective and should be stopped or changed to an alternative prophylactic agent (antibiotic).
- Consider referral to Urology at this point if not already referred.

Reviewing patients on long term prophylaxis

Patients should be reviewed after 3-6 months of prophylaxis (antibiotic or methenamine) with a review to stopping.
If prophylactic antibiotics are initiated by urology a review by urology will be required prior to stopping unless specifically discharged to the GP to carry out the review.
Urology referral details are remedy pathway (bnssgccg.nhs.uk). Consider referral if a prolonged antibiotic course is likely.

On stopping prophylaxis

Around 50% of patients will not return to suffering recurrent UTIs after stopping prophylaxis.
The patient should be given advice regarding the continuation of simple measures to prevent UTI.
Consider the use of D-mannose (for at least 6 months) and vaginal oestrogens to reduce the risk of relapse.
Providing 'standby' antibiotics when stopping continuous prophylaxis may give sufficient reassurance for patients to trial off prophylaxis.

If there is a recurrence of UTI after stopping antibiotic prophylaxis:

- Ensure the patient is complying as far as possible with the simple measures.
- If they have not already had a renal tract ultrasound and post void bladder residual volume scan consider doing this
- In post-menopausal women consider the possibility of atrophic vaginitis as a risk factor for UTI and manage appropriately.
- If appropriate investigations have been done and show no abnormality and there are no other concerning 'red flag' symptoms then continuation of prophylaxis may be considered. The ongoing need for antibiotic prophylaxis should be reviewed again after 3 months. Rotating low dose antibiotics is sometimes necessary e.g. use a different low dose antibiotic every month for three months and then go back to the original antibiotic and repeat the cycle for another three months.

Monitoring of Long-Term Nitrofurantoin

Long term nitrofurantoin usage has been associated with pulmonary and hepatotoxicity and as such the BNF advises monitoring of lung and liver function throughout the duration of treatment.

Initiation of Treatment

Prior to initiating long term (3 months or longer) nitrofurantoin for prophylaxis of UTI patients should have these undertaken and recorded at baseline:

Oxygen saturations	Chest examination	Chest X-ray (PA)
U&E	Creatinine clearance	Liver function tests
mMRC (Modified Medical Research Council) dyspnoea score (see below)		

Monitoring of Treatment

There are no pre-existing guidelines for monitoring patients prescribed long term nitrofurantoin but at a minimum we recommend patients are reviewed at 3 months and the following monitoring parameters be undertaken:

Oxygen saturations	Chest Examination	mMRC dyspnoea score (see below)	Liver function tests

A reduction in oxygen saturations, crackles or squawks on examination or deterioration in mMRC dyspnoea score should prompt an urgent repeat chest X-ray. If there are changes in interval CXR, including consolidation or interstitial changes, ensure Nitrofurantoin has been stopped and undertake a community spirometry (when able to perform after the Covid pandemic) with a follow up test at 3 months. The patient should be referred for a respiratory review and CT chest requested.

Hepatic reactions including cholestatic jaundice and chronic active hepatitis are reported. Patients should have liver function tests checked every 3 – 6 months. Treatment should be stopped at the first sign of hepatotoxicity. In such a scenario, please follow the BNSSG abnormal LFT algorithm and refer to hepatology if indicated or clinical concern.

If the patient is to continue on treatment for longer than 3 months it is recommended that monitoring recommendations repeated as outlined above on a quarterly basis.

The use of Nitrofurantoin should be reviewed at 6 months as after this period the majority of side effects occur.

mMRC Breathlessness Scale

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Chris Stenton. The MRC breathlessness scale. Occup Med (Lond)(2008)58(2): 226-227 doi:10.1093/occmed/kqm162, Table 1.
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A mMRC score of 1 or more suggests significant symptoms.

mMRC=modified Medical Research Council

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