LLR Guideline on Management of Lower Recurrent Urinary tract Infections in Adults

Definition

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

Two or more episodes of lower urinary tract infection in the last 6 months, or
Three of more lower urinary tract infection episodes in the last 12 months

This definition excludes patients with bacteriuria in the absence of symptoms or catheterised patients, i.e. asymptomatic bacteriuria. 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 treatment)[2].

A. Does the patient require urgent referral to a specialist?

Consider whether the patient requires a specialist referral for the following factors[1,3].

Red Flags for Referral to Urology:

- All men
- Frank haematuria which persists after treatment of the UTI or recurrent visible haematuria
- Neurological disease e.g., spinal cord injury, spina bifida
- Pneumaturia or faecaluria
- Proteus or Pseudomonas on urine cultures
- Urinary tract stone
- Voiding dysfunction with post-void residual >200mL on USS, or structural/functional abnormality

In Pregnancy:

- All recurrent UTIs in pregnancy should be discussed with the Obstetrics team.

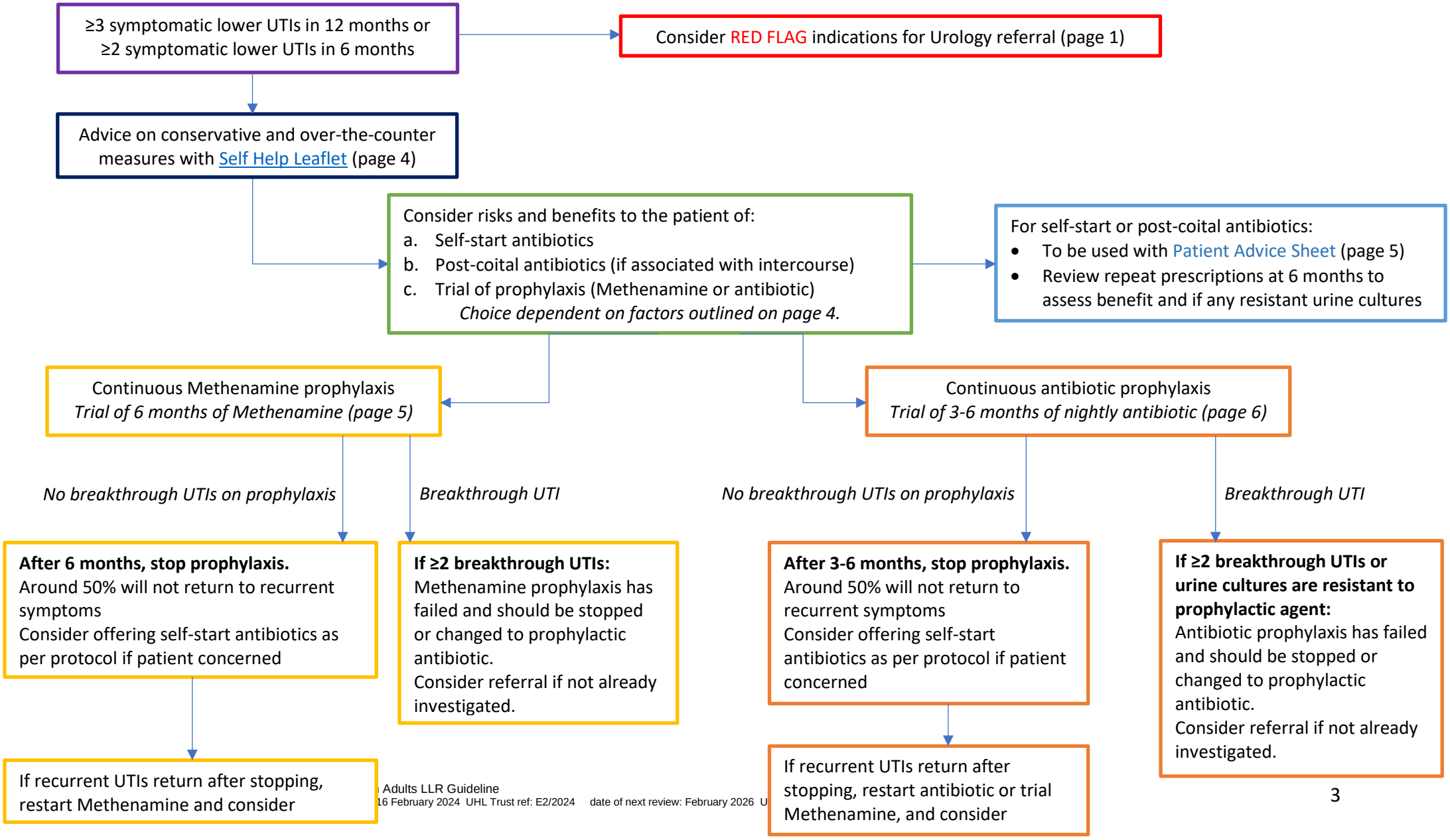
1. Patients with rUTIs should have a mid-stream urine (MSU) sample sent for culture prior to initiation of empirical antibiotics. This is to confirm infection and guide future antibiotic therapy[3].
2. Patients should be counselled on how to provide a specimen to minimise the chance of contamination using the Patient Advice Sheet*.
3. Sterile pyuria is the presence of white blood cells in the urine with no growth on routine culture.
    - In symptomatic patients with pyuria, a negative urine culture does not rule out infection[5].
    - Consider an alternative diagnosis in patients who do not respond to antibiotics as expected.
    - This can occur in several infective conditions, including sexually transmitted diseases (e.g., Chlamydia), infections with organisms that are difficult to grow on standard culture, renal tuberculosis, as well as non-infectious causes.
    - Consider a travel history, particularly to sub-Saharan Africa, to exclude schistosomiasis as a cause.
    - Symptomatic patients with persistent sterile pyuria and symptoms strongly suggestive of urinary tract infection should be discussed with the duty microbiologist.
4. Please avoid:
    - Urine cultures in the absence of symptoms. This may detect asymptomatic bacteriuria and lead to inappropriate antibiotic use, which is more likely to be harmful than beneficial[4].
    - Sending 'clearance' cultures once symptoms have resolved - these are not required.
5. Consider USS KUB including post-void residual to exclude any structural abnormalities (this is a prerequisite for secondary care referral)

C. Does the patient have any of the following risk factors which should be managed?

1. Sexual history and investigations for sexually transmitted infections should be performed if appropriate.
2. In peri- and post-menopausal women, atrophic vaginitis may cause urinary symptoms and may increase the risk of bacteriuria. Patients fitting this criteria should be offered intravaginal oestrogens[4], e.g. Vagifem or Ovestin.

* Patient Advice Sheet is available in 23 different languages here.

D. Management of recurrent UTI in non-pregnant females (to be used with full guideline below)



The following conservative measures may be advised and a Self Help Leaflet offered:

Conservative Measures:

- Drink plenty, aiming for 1.5-2L in 24 hours
- Regular voiding at least every 3-4 hourly
- Avoid use of scented washes or wipes
- For sexually active women:
    - Advise pre- and post-coital voiding
    - Avoid use of contraceptive diaphragm and spermicide
- Perineal hygiene i.e., wiping front to back.
- If using flannels, use a new clean one daily
- Advocate over-the-counter products with evidence for use:
    - D-mannose 1g twice daily (Available without prescription)
    - Cranberry tablets (Follow individual product instructions. Contraindicated in patients on Warfarin)[6]

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 should be in addition to the conservative measures detailed above and based on the patient's history and risk factors.

Summary of Prescribing Strategy Options (see detailed guidance below)	
Offer topical vaginal oestrogens in peri- and post-menopausal women, e.g. Vagifem or Ovestin. Arrange review at 6 months; if symptomatic improvement, then continue.	
Self-start antibiotics	For motivated patients with <1 UTI per month and adherent to protocol
Post-coital antibiotics	For those with a clear history of sexual intercourse precipitant
Continuous Urinary Antiseptic Prophylaxis	Continuous prophylaxis with Methenamine hippurate 1g BD
Continuous Antibiotic Prophylaxis	Continue low-dose antibiotic prophylaxis with set 3-6 month review date

Self-start Antibiotics

- Suitable for the motivated patient with <1 UTI per month.
- The Patient Advice Sheet and boric acid container for pre-antibiotic MSU should be provided to the patient.
- A urine specimen should be obtained when the patient becomes symptomatic, but patients can self-initiate antibiotics whilst awaiting the culture results.
- Prescribe a 'self-start' antibiotic according to previously known sensitivities and choose the narrowest spectrum agent available[7]. If no sensitivities available, see empirical options below.
- Safety-net with advice to seek medical attention if they develop fever, loin pain, or symptoms are not improving by 48 hours.
- Patients who are non-adherent to the protocol should not be provided with further rescue packs.

Post Coital Antibiotics

- For rUTIs triggered by sexual intercourse, this strategy is as effective as continuous antibiotic prophylaxis[8] and reduces antibiotic exposure and the risk of resistance emerging.
- Prescribe a 'self-start' antibiotic according to previously known sensitivities and choose the narrowest spectrum agent available[7] to be used as a single post-coital dose.

Continuous Urinary Antiseptic Prophylaxis (Methenamine hippurate)

- Methenamine hippurate is a urinary antiseptic agent that is converted to formaldehyde in an acidic urine environment which is directly toxic to bacteria
- A randomised control trial in 2022 demonstrated methenamine hippurate was non-inferior to prophylactic antibiotics in reducing the incidence of symptomatic UTIs over a 12-month period[9].
- Continuous methenamine prophylaxis avoids the risks of long-term prophylactic antibiotic treatment, including the development of antibiotic resistance and adverse effects such as *C. difficile* infection.
- Methenamine should be offered as a first-line alternative to continuous antibiotic therapy for UTI prevention in women.
- Methenamine should **NOT** be used for the treatment of acute UTIs.

Continuous Antibiotic Prophylaxis

- Continuous antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance.
- A **3-6 month trial** of a low-dose nightly antibiotic may be beneficial if rUTIs are occurring ≥1 UTI 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.
- Documenting and triggering a 3-6 month review date in the patient's record and on the repeat prescription is recommended to avoid prolonged courses of antibiotics without review.
- Choice of agent should be determined by previously known sensitivities and choose the narrowest spectrum agent available[7]. If no sensitivities available, see empirical options below.

Choice of Agents for Prophylaxis[6,10]:

- The choice of agent should be based on confirmed culture and sensitivity of previous urine samples, considering the patient's co-morbidities, renal function and any contra-indicating factors.
- The antibiotics licensed for the prophylaxis of UTIs are Trimethoprim and Nitrofurantoin.
- The risk of adverse effects (see box below), as well as common side-effects such as rashes, oral/vaginal thrush and gastrointestinal upset, should be discussed with the patient.

Methenamine as an alternative to antibiotics

Antiseptic	Dose	Cautions and monitoring
Methenamine	1g twice a day	• Check baseline LFTs, U&Es and eGFR. • Not for the treatment of acute UTI • Contra-indications: gout, metabolic acidosis, severe dehydration • Renal impairment: avoid if eGFR <10ml/min. • Hepatic impairment: avoid. • Pregnancy: limited safety data so preferable to avoid. • Uncommonly can cause epigastric discomfort and skin reactions

First-line antibiotic options, with a set 3-6 month review date

Antibiotic	Dose	Cautions and monitoring
Nitrofurantoin	100mg immediate release one dose post-coital (off-label) Or 50mg nightly	• Avoid if renal function eGFR <45/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 FBC, U&Es and LFTs every 3-6 months. • Advise the patient on the risk of pulmonary and hepatic fibrosis and the symptoms to report if they develop during treatment. Reactions can develop acutely or insidiously. • Advise the patient on the risk of peripheral and optic neuropathy and the symptoms to report if they develop during treatment.
Or		
Trimethoprim	200mg one dose post-coital (off-label) Or 100mg nightly	• Hyperkalaemia: caution when prescribing medications such as spironolactone, ACE inhibitor or angiotensin inhibitors • Renal impairment: avoid if eGFR <15ml/min; discuss with renal physician if eGFR <30ml/min as may increase serum creatinine. • Patient 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.

Second-line antibiotic options on Microbiology advice only

If resistance to first-line antibiotics and Methenamine, used as single agents, is not tolerated or contra-indicated, other antibiotic agents may be considered after discussion with the duty Microbiologist. Broader spectrum agents such as Cefalexin, Ciprofloxacin and Co-amoxiclav have a higher risk of *C. difficile* diarrhoea and selection for resistance, so they should not be routinely used for prophylaxis. In addition, MHRA has issued an alert restricting the use of fluoroquinolone antibiotics, e.g. Ciprofloxacin.

Second-line antibiotic option, with a set 3-6 month review date

Antibiotic	Dose	Cautions and Monitoring
Cefalexin	500mg one dose post-coital Or 125mg nightly	• Higher risk of selection for resistant infections • Higher risk of *C. difficile* infection

Managing 'breakthrough' UTIs on a continuous prophylactic agent

Methenamine prophylaxis

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

Antibiotic prophylaxis

- The first breakthrough infection should be treated according to culture and sensitivity results if available, with the original prophylaxis being held and then restarted once the infection has resolved if the culture confirms sensitivity to the prophylactic agent.
- If the culture shows resistance to the prophylactic agent, or multiple breakthrough UTIs occur, prophylaxis has therefore proved ineffective and should be stopped or changed to an alternative prophylactic agent (Methenamine or antibiotic).
- Consider referral to Urology at this point if has not already been investigated.

Managing a patient who has had a prolonged course of a continuous prophylactic agent:

Methenamine prophylaxis
Identifying patients for review:

- Patients should be reviewed after 6 months of prophylactic methenamine with a view to stopping.
- If the patient starts to suffer from recurrent UTIs again and methenamine was effective previously, this can be restarted. Consider referral for investigation (if the patient has not already been investigated)

Antibiotic prophylaxis
Identifying patients for review:

- Patients should be reviewed after 3-6 months of prophylactic antibiotics with a view to stopping or switching to Methenamine.
- Patients who have urine cultures confirming resistance to the prophylactic agent should have their prophylaxis stopped (exposure to antibiotic without benefit) and a clinical review to discuss ongoing management and/or the need for referral.

Stopping continuous prophylaxis:

It is understandable for patients to be anxious about a return to frequent UTIs after stopping continuous prophylaxis. However, a prolonged period of a prophylactic agent may allow bladder epithelial healing, reducing the risk of future UTIs when antibiotics are then stopped.

- The proportion of patients who will return to suffering recurrent UTIs after stopping continuous prophylaxis may be around 50%[8].
- This means a significant number of patients can stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of antibiotic resistance and side-effects.
- One option is to provide self-start antibiotics as per protocol when stopping continuous prophylaxis which may give sufficient reassurance to patients.
- Consider referring patients who relapse after stopping continuous prophylaxis, if not already been investigated.
- A further 3-6 month trial with Methenamine or antibiotic may be helpful in those patients whose UTIs are suppressed when on prophylaxis and recur when prophylaxis is discontinued after 6 months.

References

1. Grabe, M., Bjerklund-Johansen, T. E., Botto, H., Çek, M., Naber, K. G., & Tenke, P. (2015). Guidelines on urological infections. European Association of Urology.
2. Nicolle, L. E., Bradley, S., Colgan, R., Rice, J. C., Schaeffer, A., & Hooton, T. M. (2005). Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clinical Infectious Diseases*, 643-654.
3. NICE Clinical Knowledge Summaries: https://cks.nice.org.uk/urinary-tract-infection-lower-women#!scenario:2 accessed June 2022.
4. Scottish Intercollegiate Guideline Network. A national clinical guideline 160. Management of suspected bacterial urinary tract infection. Updated September 2020.
5. Public Health England. UK SMI B41i8.7. Updated January 2019.
6. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD001321. DOI: 10.1002/14651858.CD001321.pub5
7. Public Health England. Diagnosis of UTI. Quick Reference Guide for Primary Care. Updated May 2020.
8. Albert X, Huertas I, Pereiro I, Sanfélix J, Gosalbes V, Perrotta C. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD001209. DOI: 10.1002/14651858.CD001209.pub2
9. Harding C, Mossop H, Homer T, et al. Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial. BMJ. 2022;376:e068229. Published 2022 Mar 9. DOI:10.1136/bmj-2021-0068229
10. Urinary tract infection (recurrent): antimicrobial prescribing NICE guideline [NG112] Published date: October 2018: https://www.nice.org.uk/guidance/ng112 accessed online June 2022

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TREATING YOUR INFECTION – URINARY TRACT INFECTION (UTI)

For women under 65 years with suspected lower urinary tract infections (UTIs) or lower recurrent UTIs (cystitis or urethritis)

Possible urinary signs & symptoms

Key signs/symptoms:

Dysuria: Burning pain when passing urine (wee)
New nocturia: Needing to pass urine in the night
Cloudy urine: Visible cloudy colour when passing urine

Other signs/symptoms to consider:

Frequency: Passing urine more often than usual
Urgency: Feeling the need to pass urine immediately
Haematuria: Blood in your urine
Suprapubic pain: Pain in your lower tummy

Other things to consider:

Recent sexual history

- Inflammation due to sexual activity can feel similar to the symptoms of a UTI
- Some sexually transmitted infections (STIs) can have symptoms similar to those of a UTI

Changes during menopause

- Some changes during the menopause can have symptoms similar to those of a UTI

The outcome

Non-pregnant women:

☐ **If none or only one of: dysuria, new nocturia, cloudy urine; AND/OR vaginal discharge**

- UTI much less likely
- You may need a urine test to check for a UTI
- Antibiotics less likely to help
- Usually lasts 5 to 7 days

☐ **If 2 or more of: dysuria, new nocturia, cloudy urine; OR bacteria detected in urine; AND NO vaginal discharge**

- UTI more likely; antibiotics should help
- You should start to improve within 48 hours
- Symptoms usually last 3 days

Pregnant women: Always request urine culture

☐ **If suspected UTI**

Recommended care

☐ **Self-care and pain relief.**

- Symptoms may get better on their own

☐ **Delayed or backup prescription with self-care and pain relief**

Start antibiotics if symptoms:

- Get worse
- Do not get a little better with self-care within 48 hours

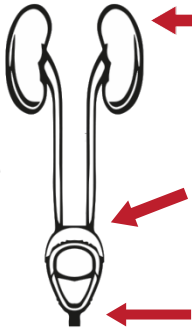
☐ **Immediate** antibiotic prescription plus self-care

☐ **If mild symptoms, delayed or back-up antibiotic prescription** plus self-care

☐ **Immediate** antibiotic prescription plus self-care

Types of urinary tract infection

UTIs are caused by bacteria getting into your urethra or bladder, usually from your gut. Infections may occur in different parts of the urinary tract.



Kidneys (make urine)
Infection in the upper urinary tract

- Pyelonephritis (pie-lo-nef-right-is). Not covered in this leaflet and always needs antibiotics

Bladder (stores urine)
Infection in the lower urinary tract

- Cystitis (sis-tight-is).

Urethra (takes urine out of the body)
Infection or inflammation in the urethra

- Urethritis (your-ith-right-is)

If you think you may have COVID-19 then please visit http://www.gov.uk/coronavirus or http://www.nhs.uk for the latest guidance and information

Self-care to help yourself get better more quickly

- Drink enough fluids to stop you feeling thirsty. Aim to drink 6 to 8 glasses
- Avoid too much alcohol, fizzy drinks or caffeine that can irritate your bladder
- Take paracetamol or ibuprofen at regular intervals for pain relief, if you have had no previous side effects
- There is currently no evidence to support taking cranberry products or cystitis sachets to improve your symptoms
- Consider the risk factors in the 'Options to help prevent UTI' column to reduce future UTIs

Options to help prevent a UTI

It may help you to consider these risk factors:

- **Stop bacteria spreading from your bowel into your bladder.** Wipe from front (vagina) to back (bottom) after using the toilet.
- **Avoid waiting to pass urine.** Pass urine as soon as you need to.
- Go for a **wee after having sex to** flush out any bacteria that may be near the opening to the urethra.
- **Wash** the external vagina area with water before and after sex to wash away any bacteria that may be near the opening to the urethra.
- **Drink** enough fluids to make sure you wee regularly throughout the day, especially during hot weather.

If you have a recurrent UTI, the following may help

- **Cranberry products and D-mannose:** There is some evidence to say that these work to help prevent recurrent UTI
- **After the menopause:** Topical hormonal treatment may help; for example, vaginal pessaries.
- Antibiotics at night or after sex may be considered

Antibiotic resistance

Antibiotics can be lifesaving. **But antibiotics are not always needed for urinary symptoms.**

↓

Antibiotics taken by mouth, **for any reason,** affect our gut bacteria making some resistant.

↓

This may make future UTI more difficult to treat

↓

Common **side effects** to taking antibiotics include thrush, rashes, vomiting and diarrhoea. Seek medical advice if you are worried.

↓

Keep antibiotics working; only take them when advised by a health professional. This way they are more likely to work for a future UTI.

When should you get help?

Contact your GP practice or contact NHS

The following symptoms are possible signs of serious infection and should be assessed urgently.

Phone for advice if you are not sure how urgent the symptoms are.

1. You have shivering, chills and muscle pain
2. You feel confused, or are very drowsy
3. You have not passed urine all day
4. You are vomiting
5. You see blood in your urine
6. Your temperature is above 38°C or less than 36°C.
7. You have kidney pain in your back just under the ribs
8. Your symptoms get worse
9. Your symptoms are not starting to improve within 48 hours of taking antibiotics

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Self-Management and Rescue Pack Advice Sheet

You have been provided with a red-top urine sample pot and a rescue pack of antibiotics.

What to do if you experience urinary tract infection symptoms:

1. Collect a mid-stream sample of your urine in the sample pot provided.
2. Place the pot of urine in a sealed plastic bag and hand in to the GP reception straight away. If there is a delay, store in the fridge and hand in on the next working day.
3. Take the first dose of the antibiotic supplied.
4. Follow the instructions for taking the full course of antibiotics.
5. Contact your GP practice to discuss the results of the urine culture (usually available 24-72 hours after handed into the practice), and to obtain a new sample pot and rescue pack of antibiotics. The GP will check whether the same antibiotics are still appropriate for your next rescue pack (if the antibiotic will still work against the bacteria in the urine).

What to do if the symptoms of urinary tract infection do not improve:
Your symptoms should start to improve once you start taking the antibiotics. If you have not improved within 48 hours, or the symptoms have got worse, or you feel feverish, develop new back pain or feel generally unwell, contact the GP practice, or call 111 if the GP practice is shut.

	Date of start of symptoms	Date urine sample provided	Date of start of antibiotics (if given)	Date symptoms settled
1				
2				
3				
4				

How should I collect a urine sample?

You should:

- Collect your pee (urine) sample in a completely clean (sterile) container.
- Store it in a fridge in a sealed plastic bag if you can't hand it in straight away.

Collecting a urine sample

- Your doctor or another healthcare professional should give you a container and explain how you should collect the urine sample.
- You can collect a urine sample at any time of day, unless your GP or practice nurse advises you otherwise.
- The types of urine sample you might be asked for include a random specimen, first morning specimen or timed collection.
- To collect a urine sample you should:
  1. Label a sterile, screw-top container with your name, date of birth and the date
  2. Wash your hands
  3. Start to pee and collect a sample of urine "mid-stream" in the container
  4. Screw the lid of the container shut
  5. Wash your hands thoroughly
  6. Follow any other instructions your doctor has given you.

What is a mid-stream urine sample?
A mid-stream urine sample means you don't collect the first or last part of urine that comes out. This reduces the risk of the sample being contaminated with bacteria from:

- your hands
- the skin around the urethra, the tube that carries urine out of the body

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