

Urinary tract infection (lower) - women - Management

Scenario: Cystitis in women who are not pregnant

How should I manage a woman with suspected cystitis?

- **Convey a positive approach** and reassure the woman that cystitis is generally self-limiting.
 - Without antibiotics, symptoms can be expected to resolve in 4–9 days.
 - With antibiotics, symptoms can be expected to resolve in 3–8 days.
 - On average, antibiotics shorten the duration of symptoms by about a day.
- **Relieve symptoms** with [paracetamol](#) or [ibuprofen](#) — do *not* recommend urine alkalinizing agents or cranberry products.
- **If cystitis symptoms are moderate or severe:**
 - Offer an [antibiotic](#).
 - Do not dipstick test the urine, as the decision to offer an antibiotic is not influenced by urine dipstick test results. Even if the tests for nitrite, *and* leucocyte esterase, *and* blood are all negative, an antibiotic should still be offered.
 - If the woman prefers not to take an antibiotic, offer a delayed antibiotic prescription to be dispensed if the symptoms become worse, or last more than 48 hours.
- **If cystitis symptoms are mild:**
 - Dipstick test the urine to guide treatment decisions.
 - Discuss not using an antibiotic, especially if the urine dipstick test is negative for nitrites *and* leucocyte esterase *and* blood.
 - Have a lower threshold for offering an antibiotic if there are [risk factors](#) for persistent infection, recurrent infection, or treatment failure.
 - If there are concerns about not taking an antibiotic, offer a delayed antibiotic prescription to be dispensed if the symptoms become worse, or last more than 48 hours.
- **Advise the woman to seek medical attention if she develops a high fever or becomes systemically unwell.**

[In depth](#)

When prescribing empirically for acute cystitis which antibiotic should I choose?

- Follow local guidelines when available.
- If local guidelines are not available:
 - For an uncomplicated infection, prescribe either:
 - [Trimethoprim](#) 200 mg twice daily, for 3 days, *or*
 - [Nitrofurantoin](#) 50 mg four times daily, or 100 mg (modified-release) twice daily, for 3 days.
 - For a [complicated](#) infection, prescribe a 5–10-day course of trimethoprim or nitrofurantoin.

[In depth](#)

When should I culture the urine of a woman with suspected cystitis?

- Urine microscopy and culture are not routinely required for women with uncomplicated cystitis.
- Send urine for microscopy and culture if any of the following apply:
 - There are risk factors for a [complicated](#) urinary tract infection — for example the woman has recently had urological instrumentation, or is immunocompromised, or has been in hospital recently.
 - Confirmation of the [diagnosis](#) or exclusion of [other conditions](#) is required.
 - The woman has not responded to antibiotic treatment.
 - The woman has recurrent episodes of cystitis and this has not been investigated.
 - When underlying causes of recurrent cystitis and other conditions have been excluded, it is not necessary to routinely culture the urine for further episodes.

[In depth](#)

How should I follow up a woman with cystitis?

- Follow up is not routinely required for uncomplicated cystitis, but should be considered for women with a potentially [complicated](#) infection.
- If haematuria was found, follow up to re-test the urine and check that the infection and haematuria have resolved.

[In depth](#)

When should I refer a woman with acute cystitis?

- If the woman fails to respond to two courses of antibiotics shown by urine culture results to be appropriate treatment, refer for specialist assessment.
- If [urological cancer](#) is suspected (for example haematuria persists after successful treatment of cystitis), refer urgently to a team specializing in the management of urological cancer.

[In depth](#)

How should I manage a woman whose cystitis has failed to respond to antibiotics?

- Continue symptomatic treatment with paracetamol or ibuprofen.
- Check compliance with antibiotic treatment.
- Send a urine sample for culture.
- If symptoms are troublesome, offer a different antibiotic (nitrofurantoin or trimethoprim) while waiting for the culture results — see [Choice of antibiotic](#).
- **If infection is confirmed on culture**, treat with an antibiotic to which the organism is sensitive.
- **If infection is not confirmed on culture**, consider other possible causes for the symptoms — see [Differential diagnosis](#).
- **If cystitis symptoms fail to respond to two courses of antibiotic shown by culture to be appropriate treatment**, refer for specialist assessment.

[In depth](#)

Prescriptions

Antibiotic treatment (UTI): trimethoprim and nitrofurantoin

Age from 14 years onwards

Trimethoprim tablets: 200mg twice a day for 3 days

Trimethoprim 200mg tablets
Take one tablet twice a day for 3 days.
Supply 6 tablets.

Age: from 14 years onwards
NHS cost: £0.39
Licensed use: yes

Trimethoprim tablets: 200mg twice a day for 7 days

Trimethoprim 200mg tablets

Take one tablet twice a day for 7 days.
Supply 14 tablets.

Age: from 14 years onwards
NHS cost: £0.91
Licensed use: yes

Nitrofurantoin tablets: 50mg four times a day for 3 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 3 days.
Supply 12 tablets.

Age: from 14 years onwards
NHS cost: £1.21
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin tablets: 50mg four times a day for 7 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 7 days.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £2.83
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 3 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 3 days.
Supply 12 capsules.

Age: from 14 years onwards
NHS cost: £1.00
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 7 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 7 days.
Supply 28 capsules.

Age: from 14 years onwards
NHS cost: £2.32
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 3 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 3 days.
Supply 6 capsules.

Age: from 14 years onwards
NHS cost: £2.10
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 7 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 7 days.
Supply 14 capsules.

Age: from 14 years onwards
NHS cost: £4.89
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Analgesia: use when required

Age from 16 years onwards

Ibuprofen tablets: 200mg to 400mg three to four times a day

Ibuprofen 200mg tablets
Take one or two tablets 3 to 4 times a day when required for pain relief. Do not exceed the stated dose.
Supply 56 tablets.

Age: from 16 years onwards
NHS cost: £1.38
OTC cost: £2.38
Licensed use: yes

Paracetamol tablets: 500mg to 1g up to four times a day

Paracetamol 500mg tablets
Take one or two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.
Supply 50 tablets.

Age: from 16 years onwards
NHS cost: £0.78
OTC cost: £1.35
Licensed use: yes

Urinary tract infection (lower) - women - Management

Scenario: Recurrent cystitis in women who are not pregnant

How should I manage an acute episode of recurrent cystitis?

- Review the diagnosis.
- Culture the urine to confirm infection and exclude [other causes](#).
- Refer urgently if [urological cancer](#) is suspected.
- Review the woman's medical and surgical history to assess risk factors for recurrent cystitis such as stones, papillary necrosis, and vesicoureteric reflux — this assessment may require imaging and urological referral.
- Relieve symptoms with [paracetamol](#) or [ibuprofen](#).
- If symptoms are moderate or severe, offer an [antibiotic](#) immediately.

- If symptoms are mild, suggest delaying antibiotic treatment until culture results are available to guide choice of antibiotic.
- Advise on [lifestyle measures](#) such as high-strength cranberry capsules to reduce the risk of recurrent episodes.
- If troublesome cystitis recurs frequently:
 - Consider offering a prescription for a 'stand-by' antibiotic to be used for future episodes.
 - Consider [preventive treatments](#).
- [Refer](#) or seek specialist advice if these measures are not successful.

[In depth](#)

[Which antibiotic should I prescribe for a woman with recurrent cystitis?](#)

- Follow local guidelines when available. Otherwise:
 - For empirical treatment, prescribe either:
 - Trimethoprim 200 mg twice daily, for 3 days, *or*
 - Nitrofurantoin 50 mg four times daily, or 100 mg (modified-release) twice daily, for 3 days.
 - If the woman has been treated with trimethoprim recently (up to a year previously), consider prescribing nitrofurantoin instead of trimethoprim.

[In depth](#)

[What lifestyle measures should I advise for preventing cystitis?](#)

Advise women with recurrent cystitis that:

- Cranberry products reduce the recurrence rate of cystitis, and are available from shops (but not on the NHS).
 - Cranberry products should not be taken if warfarin is being used.
 - High strength capsules (containing at least 200 mg of cranberry extract) are recommended because they may be more effective and acceptable than cranberry juice.
- If cystitis is related to sexual intercourse, advise:
 - Using a different contraceptive method if a diaphragm is being used.

- Voiding soon after intercourse.
- Using a lubricant if symptoms could be due to mild trauma rather than infection.

[In depth](#)

When should I offer preventive treatments for recurrent cystitis?

- Consider offering a prescription for a 'stand-by' antibiotic to be used for future episodes of cystitis before prescribing prophylactic drug treatment.
- When deciding to offer prophylactic drug treatment, consider the frequency, severity, and impact of recurrent cystitis, and whether referral for urological investigation would be appropriate.
- For recurrent cystitis associated with sexual intercourse, offer trimethoprim 100 mg to be taken within 2 hours of intercourse (off-label use).
- For recurrent cystitis not associated with sexual intercourse offer a 6-month trial of low-dose continuous antibiotic treatment: trimethoprim 100 mg every night, or nitrofurantoin (immediate-release) 50–100 mg every night.

[In depth](#)

How should I follow up a woman with recurrent cystitis?

- If prophylactic antibiotics are prescribed, follow up to review progress after 6 months, or sooner if clinically indicated.
- If haematuria was found, follow up to re-test the urine and check that the infection and haematuria have resolved.

[In depth](#)

When should I refer a woman with recurrent cystitis?

- Refer urgently, to a team specializing in the management of urological cancer, if [urological cancer](#) is suspected (for example if haematuria persists after successful treatment of acute cystitis).
- Refer the woman if:
 - Risk factors for recurrent cystitis (such as urinary tract abnormalities, stones, vesicoureteric reflux, papillary necrosis) are present or suspected.
 - There is any known abnormality on ultrasound of kidneys, ureters, and bladder.

- o The response to preventive treatments and lifestyle measures is ineffective.

[In depth](#)

Prescriptions

Antibiotic treatment (UTI): trimethoprim and nitrofurantoin

Age from 14 years onwards

Trimethoprim tablets: 200mg twice a day for 3 days

Trimethoprim 200mg tablets
Take one tablet twice a day for 3 days.
Supply 6 tablets.

Age: from 14 years onwards
NHS cost: £0.39
Licensed use: yes

Trimethoprim tablets: 200mg twice a day for 7 days

Trimethoprim 200mg tablets
Take one tablet twice a day for 7 days.
Supply 14 tablets.

Age: from 14 years onwards
NHS cost: £0.91
Licensed use: yes

Nitrofurantoin tablets: 50mg four times a day for 3 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 3 days.
Supply 12 tablets.

Age: from 14 years onwards
NHS cost: £1.21
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin tablets: 50mg four times a day for 7 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 7 days.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £2.83
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 3 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 3 days.
Supply 12 capsules.

Age: from 14 years onwards
NHS cost: £1.00
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 7 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 7 days.
Supply 28 capsules.

Age: from 14 years onwards
NHS cost: £2.32
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 3 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 3 days.
Supply 6 capsules.

Age: from 14 years onwards
NHS cost: £2.10
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 7 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 7 days.
Supply 14 capsules.

Age: from 14 years onwards
NHS cost: £4.89
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Antibiotic prophylaxis for recurrent UTIs

Age from 14 years onwards

Trimethoprim tablets: 100mg at night

Trimethoprim 100mg tablets
Take one tablet at night.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £0.98
Licensed use: yes

Nitrofurantoin tablets: 50mg at night

Nitrofurantoin 50mg tablets
Take one tablet at night.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £2.48
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg at night

Nitrofurantoin 50mg capsules

Take one capsule at night.
Supply 28 capsules.

Age: from 14 years onwards
NHS cost: £2.32
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin tablets: 100mg at night

Nitrofurantoin 100mg tablets
Take one tablet at night.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £4.34
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 100mg at night

Nitrofurantoin 100mg capsules
Take one capsule at night.
Supply 30 capsules.

Age: from 14 years onwards
NHS cost: £4.81
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Antibiotic prophylaxis: post-coital

Age from 16 years onwards

Trimethoprim tablets: 100mg post-coital

Trimethoprim 100mg tablets
Take one tablet within 2 hours of intercourse.
Supply 28 tablets.

Age: from 16 years onwards
NHS cost: £0.99
Licensed use: no - off-label indication

Analgesia: use when required

Age from 16 years onwards

Ibuprofen tablets: 200mg to 400mg three to four times a day

Ibuprofen 200mg tablets
Take one or two tablets 3 to 4 times a day when required for pain relief. Do not exceed the stated dose.
Supply 56 tablets.

Age: from 16 years onwards
NHS cost: £1.38
OTC cost: £2.38
Licensed use: yes

Paracetamol tablets: 500mg to 1g up to four times a day

Paracetamol 500mg tablets

Take one or two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.
Supply 50 tablets.

Age: from 16 years onwards

NHS cost: £0.78

OTC cost: £1.35

Licensed use: yes

Urinary tract infection (lower) - women - Management

Scenario: Asymptomatic bacteriuria and cystitis in women who are pregnant

How should I screen for and manage asymptomatic bacteriuria during pregnancy?

- **Screen for asymptomatic bacteriuria** on the first antenatal visit by sending urine for culture. If asymptomatic bacteriuria is found, send a second urine sample for culture.
- **If the second urine culture confirms asymptomatic bacteriuria**, treat for 7 days with an antibiotic to which the organism is sensitive.
 - Preferred options when sensitivities are known are (in order of preference):
 - Amoxicillin: 250 mg three times daily, for 7 days.
 - Nitrofurantoin: 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
 - Trimethoprim: 200 mg twice daily, for 7 days (unless the woman is folate deficient or taking a folate antagonist).
 - Cefalexin (500 mg twice daily, or 250 mg 6-hourly, for 7 days) may be used but is less preferred.
- After treatment, send urine for culture to screen for asymptomatic bacteriuria at every antenatal visit until delivery.
- **If a group B streptococcus is isolated**, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

[In depth](#)

Cystitis in pregnancy

How should I manage a pregnant woman with suspected acute cystitis?

- Convey a positive approach and reassure the woman that treatment with an antibiotic will prevent any harm to her baby, and will shorten the duration of symptoms.

- If the woman has fever or loin tenderness, suspect upper urinary tract infection and admit or seek urgent specialist opinion.
- Offer [paracetamol](#) for symptomatic relief. Do not recommend urine alkalinizing agents or cranberry products. Do not recommend urine alkalinizing agents or cranberry products.
- Send a urine sample for culture before starting antibiotic treatment.
- Prescribe an antibiotic empirically. If local guidelines are not available, suitable first-line antibiotics are (in order of preference):
 - Nitrofurantoin 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
 - Trimethoprim 200 mg twice daily, for 7 days (if the person is not folate deficient or taking a folate antagonist, and has not been treated with trimethoprim in the past year).
 - Cefalexin 500 mg twice daily, or 250 mg 6-hourly, for 7 days.
- [Follow up](#) after 48 hours (or according to the clinical situation) to check response to treatment and the urine culture results.
- Amoxicillin 250 mg three times daily, for 7 days, is recommended only if the organism is reported to be susceptible on the culture results.

[In depth](#)

How should I follow up a pregnant woman with cystitis?

- Review culture results when available and, if necessary, change to an antibiotic that the organism is sensitive to.
- Send urine cultures to screen for asymptomatic bacteriuria 7 days after completion of treatment, and at every antenatal visit until delivery.
- **If a group B streptococcus is isolated**, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

[In depth](#)

When should I refer a pregnant woman with cystitis?

- Admit, or seek urgent specialist opinion, if upper urinary tract infection is suspected (fever, loin tenderness, and pain).

- Seek specialist advice if symptoms fail to respond to antibiotic treatment guided by urine culture results, and if other causes have been excluded — see [Differential diagnosis](#).

[In depth](#)

How should I manage a pregnant woman whose cystitis has failed to respond to antibiotics?

- Check compliance with antibiotic treatment.
- Continue symptomatic treatment with paracetamol or, in the first or second trimesters, ibuprofen.
- Send a urine sample for culture.
- If symptoms are troublesome, offer a different antibiotic (nitrofurantoin or trimethoprim) while waiting for the culture results — see [Managing suspected acute cystitis during pregnancy](#).
- **If infection is confirmed on culture**, treat with an antibiotic to which the organism is sensitive.
- **If infection is not confirmed on culture**, consider other possible causes for the symptoms — see [Differential diagnosis](#).
- **If cystitis symptoms fail to respond to a second antibiotic shown by urine culture results to be appropriate treatment**, seek specialist advice.

[In depth](#)

Prescriptions

Antibiotics: urinary tract infection in pregnancy

Age from 14 years onwards

Nitrofurantoin tablets: 50mg four times a day for 7 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 7 days.
Supply 28 tablets.

Age: from 14 years onwards

NHS cost: £2.83

Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 7 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 7 days.
Supply 28 capsules.

Age: from 14 years onwards

NHS cost: £2.32

Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 7 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 7 days.
Supply 14 capsules.

Age: from 14 years onwards

NHS cost: £4.89

Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Trimethoprim tablets: 200mg twice a day for 7 days

Trimethoprim 200mg tablets
Take one tablet twice a day for 7 days.
Supply 14 tablets.

Age: from 14 years onwards

NHS cost: £0.91

Licensed use: yes

Cefalexin tablets: 250mg four times a day for 7 days

Cefalexin 250mg tablets
Take one tablet four times a day for 7 days.
Supply 28 tablets.

Age: from 14 years onwards

NHS cost: £2.19

Licensed use: yes

IF known to be sensitive: amoxicillin 250mg three times a day for 7 days

Amoxicillin 250mg capsules
Take one capsule three times a day for 7 days.
Supply 21 capsules.

Age: from 14 years onwards

NHS cost: £0.62

Licensed use: yes

Cefalexin tablets: 500mg twice a day for 7 days

Cefalexin 500mg tablets
Take one tablet twice a day for 7 days.
Supply 14 tablets.

Age: from 14 years onwards

NHS cost: £1.79

Licensed use: yes

Analgesia: use when required (paracetamol only)

Age from 14 years onwards

Paracetamol tablets: 500mg to 1g up to four times a day

Paracetamol 500mg tablets
Take one or two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.
Supply 50 tablets.

Urinary tract infection (lower) - women - Management

Scenario: Lower urinary tract infection in women with a chronic indwelling urinary catheter

How should I treat lower UTI in a woman with an indwelling catheter?

- **Do not treat asymptomatic bacteriuria.**
- Remember that considerable clinical judgement is required to [diagnose](#) urinary tract infection (UTI) in women with an indwelling urinary catheter.
- If symptoms are severe (for example, severe nausea and vomiting, confusion, tachypnoea, tachycardia, hypotension, reduced urine output), admit to hospital as intravenous antibiotics may be required.
- Check that the catheter is correctly positioned and not blocked.
 - If the catheter has been in place for more than a week, consider changing it before starting antibiotic treatment.
- If there is fever, or loin pain, or both, manage as upper UTI, see the CKS topic on [Pyelonephritis - acute](#).
- Otherwise, treat for lower UTI:
 - Relieve symptoms with [paracetamol](#) or [ibuprofen](#).
 - Send urine for culture and microscopy before starting antibiotic treatment.
 - Prescribe an antibiotic for 7 days, following local guidelines when available.
 - If symptoms are mild, consider withholding antibiotics until the result of urine culture is available to guide choice of antibiotic.
 - If symptoms are moderate or severe, [empirically](#) prescribe an antibiotic.
 - [Follow up](#) after 48 hours (or according to the clinical situation) to check response to treatment and the result of urine culture.

[In depth](#)

Which antibiotic should I prescribe empirically for UTI in a woman with an indwelling urinary catheter?

- Follow local guidelines when available. Otherwise:
 - For empirical treatment, prescribe either:
 - Trimethoprim 200 mg twice daily, for 7 days, *or*
 - Nitrofurantoin 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
 - If the woman has a history of recurrent infections, or has recently (within the past year) taken trimethoprim, do not use trimethoprim for empirical treatment.

[In depth](#)

How can I prevent urinary tract infections in women with indwelling catheters?

- **Ensure an indwelling urinary catheter is appropriate.**
 - Use an indwelling catheter only after alternative methods of management have been considered.
 - Regularly review the clinical need for catheterization and remove the catheter as soon as possible.
 - Use intermittent catheterization in preference to an indwelling catheter if this is clinically appropriate and is a practical option for the person.
- **Prevent the introduction of infection.**
 - Healthcare personnel should be trained and assessed in their competence to perform urethral catheterization using aseptic procedures.
 - Urine samples should be obtained from a sampling port using an aseptic technique.
 - Catheters should be changed only when clinically necessary (for example, to prevent blockage), or according to the manufacturer's recommendations.
 - When changing catheters, antibiotic prophylaxis should only be used for people with a history of catheter-associated urinary tract infection following catheter change.
- **Do not use:**
 - Bladder instillations or washouts.
 - Prophylactic antibiotics when changing catheters in women with a heart valve lesion, septal defect, patent ductus, or prosthetic valve.

- o Topical antiseptics or antibiotics applied to the catheter, urethra, or meatus; daily washing of the meatus with soap and water is sufficient.

[In depth](#)

How should I follow up a woman with an indwelling catheter and treated for UTI?

- Review after 48 hours, or according to the clinical situation, to ensure the woman is responding to treatment, and to check the results of the urine culture.
- If urine culture shows that the organism is resistant to the current antibiotic, and:
 - o If symptoms have not resolved, change to an antibiotic that the organism is sensitive to.
 - o If symptoms have resolved, consider continuing with the current antibiotic.
 - o If symptoms recur, start treat with an antibiotic shown in the culture to cover the infecting organism.
- If the woman fails to respond to two courses of antibiotic shown by urine culture to be appropriate treatment, and compliance has been checked, consider referring for assessment and investigation.

[In depth](#)

When should I refer a woman with an indwelling catheter and treated for UTI?

- Consider referring for assessment and investigation if the woman fails to respond to two courses of antibiotic shown by urine culture to be appropriate treatment, and compliance has been verified.
- If [urological cancer](#) is suspected (for example if haematuria persists after successful treatment of cystitis), refer urgently to a team specializing in the management of urological cancer.

[In depth](#)

Prescriptions

Antibiotics: UTI in women with catheters

Age from 14 years onwards

Trimethoprim tablets: 200mg twice a day for 7 days

Trimethoprim 200mg tablets
 Take one tablet twice a day for 7 days.
 Supply 14 tablets.

Age: from 14 years onwards
NHS cost: £0.91
Licensed use: yes

Nitrofurantoin tablets: 50mg four times a day for 7 days

Nitrofurantoin 50mg tablets
Take one tablet four times a day for 7 days.
Supply 28 tablets.

Age: from 14 years onwards
NHS cost: £2.83
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin capsules: 50mg four times a day for 7 days

Nitrofurantoin 50mg capsules
Take one capsule four times a day for 7 days.
Supply 28 capsules.

Age: from 14 years onwards
NHS cost: £2.32
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Nitrofurantoin m/r caps: 100mg twice a day for 7 days

Nitrofurantoin 100mg modified-release capsules
Take one capsule twice a day for 7 days.
Supply 14 capsules.

Age: from 14 years onwards
NHS cost: £4.89
Licensed use: yes

Patient information: This medicine may cause your urine to turn more yellow than normal.

Analgesia: use when required

Age from 16 years onwards

Ibuprofen tablets: 200mg to 400mg three to four times a day

Ibuprofen 200mg tablets
Take one or two tablets 3 to 4 times a day when required for pain relief. Do not exceed the stated dose.
Supply 56 tablets.

Age: from 16 years onwards
NHS cost: £1.38
OTC cost: £2.38
Licensed use: yes

Paracetamol tablets: 500mg to 1g up to four times a day

Paracetamol 500mg tablets
Take one or two tablets every 4 to 6 hours when required for pain relief. Maximum of 8 tablets in 24 hours.
Supply 50 tablets.

Age: from 16 years onwards
NHS cost: £0.78
OTC cost: £1.35
Licensed use: yes

Urinary tract infection (lower) - women - Management

Detailed answers

Overview of management

Acute cystitis in non-pregnant women

- Convey a positive approach and reassure the woman that cystitis is generally self-limiting.
- Relieve the symptoms with paracetamol or ibuprofen.
- If cystitis symptoms are moderate or severe, offer a 3-day course of:
 - Trimethoprim 200 mg twice daily, *or*
 - Nitrofurantoin 50 mg four times a day, or 100 mg (modified-release) twice daily.
- If cystitis symptoms are mild:
 - Dipstick test the urine and if results are negative, discuss not treating the cystitis with an antibiotic.
 - Have a lower threshold for offering an antibiotic if there are risk factors for persistent infection, recurrent infection, or treatment failure.
 - If there are concerns about not taking an antibiotic, offer a delayed antibiotic prescription to be dispensed if the symptoms become worse, or last more than 48 hours.
- Urine culture is not routinely required.
 - Urine culture is useful to confirm the diagnosis and to guide choice of antibiotic when there are risk factors for more severe illness or treatment has failed.
- If cystitis symptoms fail to respond to an antibiotic chosen according to the urine culture result, check compliance, repeat the urine culture, change to another antibiotic, and consider referring for specialist assessment.

Recurrent cystitis

- Review the diagnosis.
- Review the medical and surgical history to assess risk factors for recurrent cystitis such as stones, papillary necrosis, and vesicoureteric reflux — this may require imaging or urological referral.
- Relieve the symptoms with paracetamol or ibuprofen.
- Treat the infection with a 3-day course of trimethoprim or nitrofurantoin (as above) if the symptoms are severe.

- Advise on lifestyle measures for prevention, such as use of cranberry products. High strength (at least 200 mg) capsules may be more effective and better tolerated than cranberry drinks.
- For women with troublesome recurrent cystitis, consider:
 - A prescription for a 'stand-by' antibiotic to be used for future episodes of cystitis.
 - Trimethoprim 200 mg to be taken within 2 hours of intercourse (off-label use).
 - A 6-month trial of low-dose continuous antibiotic treatment: trimethoprim 100 mg or nitrofurantoin (immediate-release) 50–100 mg, every night.

Asymptomatic bacteriuria in pregnancy

- Screen for asymptomatic bacteriuria on the first antenatal visit by sending urine for culture.
- If asymptomatic bacteriuria is found, send a second urine sample for culture.
- If the second urine culture confirms asymptomatic bacteriuria, treat for 7 days with an antibiotic to which the organism is sensitive. Do not use trimethoprim first-line if there is a suitable alternative.
- After treatment, send urine for culture to screen for asymptomatic bacteriuria at every antenatal visit until delivery.
- If a group B streptococcus is isolated, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

Cystitis during pregnancy

- Culture the urine.
- Relieve the symptoms with paracetamol.
- Treat the infection with an appropriate antibiotic for 7 days (in order of preference: nitrofurantoin, trimethoprim [if the woman is not folate deficient or taking a folate antagonist], amoxicillin, cefalexin).
- Have a low threshold for admitting the woman if upper urinary tract infection (UTI) is suspected (fever, loin tenderness, and pain).
- After treatment, send urine for culture to screen for asymptomatic bacteriuria at every antenatal visit until delivery.
- If a group B streptococcus is isolated, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

Lower UTI in women with an indwelling urinary catheter

- For women with an indwelling urinary catheter, considerable clinical judgement is required to diagnose UTI.
- Assess the severity of the infection and the presence of any comorbidities.
- Admit the woman to hospital if there are symptoms and signs of severe infection.
- If there is fever, and flank pain or tenderness, manage as for upper UTI — see the CKS topic on [Pyelonephritis - acute](#).
- Check that the catheter is correctly positioned and not blocked.
- Send urine for culture before antibiotic treatment is started.
- If it is practical, withhold antibiotics until the result of urine culture is available to guide the choice of antibiotic. Otherwise, empirically prescribe trimethoprim or nitrofurantoin for 7 days.
- Relieve the symptoms with paracetamol or ibuprofen.
- Check the urine culture report. If necessary, change the antibiotic to one to which the organism is sensitive.
- To prevent UTI:
 - Use an indwelling urinary catheter only after alternative methods of management have been considered, and regularly review the need for a catheter.
 - Ensure high standards of hygiene with catheter care: obtain urine samples from a sampling port using an aseptic technique, and change catheters only when necessary.
 - When changing catheters, only use antibiotic prophylaxis for people with a history of catheter-associated UTI following catheter change.

Acute cystitis (not pregnant)

How should I manage a woman with suspected cystitis?

- **Convey a positive approach** and reassure the woman that cystitis is generally self-limiting:
 - Without antibiotics, symptoms can be expected to resolve in 4–9 days.
 - With antibiotics, symptoms can be expected to resolve in 3–8 days.
 - On average, antibiotics shorten the duration of symptoms by about a day.

- **Relieve symptoms** with [paracetamol](#) or [ibuprofen](#) — do not recommend urine alkalinizing agents or cranberry products.
- **If cystitis symptoms are moderate or severe:**
 - Offer an [antibiotic](#).
 - Do not dipstick test the urine, as the decision to offer an antibiotic is not influenced by urine dipstick test results. Even if the tests for nitrite, *and* leucocyte esterase, *and* blood are all negative, an antibiotic should still be offered.
 - If the woman prefers not to take an antibiotic, offer a delayed antibiotic prescription to be dispensed if the symptoms become worse, or last more than 48 hours.
- **If cystitis symptoms are mild:**
 - Dipstick test the urine to guide treatment decisions.
 - Discuss not using an antibiotic, especially if the urine dipstick test is negative for nitrites *and* leucocyte esterase *and* blood.
 - Have a lower threshold for offering an antibiotic if there are [risk factors](#) for persistent infection, recurrent infection, or treatment failure.
 - If there are concerns about not taking an antibiotic, offer a delayed antibiotic prescription to be dispensed if the symptoms become worse, or last more than 48 hours.
- **Advise the woman to seek medical attention if she develops a high fever or becomes systemically unwell.**

Basis for recommendation

These recommendations are in line with Scottish [[SIGN, 2006](#)], European [[European Association of Urology, 2009](#)], and American [[ICSI, 2004](#); [American College of Obstetricians and Gynecologists, 2008](#)] guidelines. The recommendations also take into account the evidence from a Health Technology Assessment (HTA) commissioned by the National Institute for Health Research (NIHR) to assess the diagnosis of cystitis, its prognosis, and five different treatment strategies [[Little et al, 2009](#)].

A positive approach to prognosis

- A positive approach to diagnosis and prognosis has been found to be independently associated with shorter duration of symptoms in observational studies and in randomized controlled trials [[Thomas, 1987](#); [Little et al, 2001](#); [Little et al, 2009](#)].
- The average duration of symptoms (that are at least moderately severe) is reported in the NIHR HTA [[Little et al, 2009](#)] and summarized in the [Prognosis](#) section.

Use of an analgesic for symptomatic relief

- CKS found no trials of analgesics for the painful symptoms of cystitis. The recommendation to use paracetamol or ibuprofen to treat the painful symptoms of cystitis is based on their use in other painful infections and the experience of experts [[SIGN, 2006](#)].
- There is insufficient evidence to recommend the use of:
 - [Urine alkalinizing agents](#) (such as potassium citrate or bicarbonate): CKS found no controlled trials of urine alkalinizing agents. One observational study found no relationship between symptoms of cystitis and urine pH [[Brumfitt et al, 1990](#)].
 - [Cranberry products](#): a Cochrane systematic review found no good evidence to support the use of cranberry juice or other cranberry products for *treating* acute UTIs [[Jepson et al, 1998](#)].

Treatment strategy (to consider the options of an antibiotic, no antibiotic, or delayed antibiotic prescription)

- The evidence that a course of antibiotics is effective is discussed in [Choice of antibiotic](#).
- The strategy for antibiotic prescribing is supported by [evidence](#) from a series of studies in the UK [[Little et al, 2009](#)], and a randomized controlled trial in New Zealand [[Richards et al, 2005](#)].
- No clinically (or economically) important differences were found between five different treatment strategies in which antibiotics were offered: (i) immediately, (ii) delayed for 48 hours, (iii) according to a symptom rule, (iv) according to a dipstick test rule, or (v) according to the results of urine culture.
- Women who did not meet the criteria for immediate antibiotic treatment were offered a delayed antibiotic prescription to use if their symptoms did not settle after 48 hours. In each group where women were offered a delayed prescription, a high proportion chose to use it.
- Women who presented with more severe symptoms of dysuria, urgency, frequency, and nocturia recovered more slowly.
- Antibiotics shortened the duration of symptoms (that were at least moderately severe) by about 1–2 days.

- CKS therefore recommends offering an antibiotic when:
 - Presenting symptoms are moderate or severe — because antibiotics are likely to shorten the duration of symptoms by 1–2 days.
 - The woman has a strong preference for antibiotic treatment — because there is no evidence that treatment leads to poorer outcomes, although there is also no evidence of effectiveness in women with less severe symptoms.
 - It may be a [complicated](#) infection — because there is a greater risk of adverse effects from infection.
- While CKS recommends using *severity* of symptoms as a key decision criterion, other guidelines (for example [[SIGN, 2006](#)]) recommend using *number* of symptoms.
- CKS recommends considering a delayed antibiotic prescription whenever an antibiotic is not prescribed, because this may give some women the confidence needed to try not using an antibiotic, to see if the symptoms resolve spontaneously.

When prescribing empirically for acute cystitis which antibiotic should I choose?

- **Follow local guidelines when available.**
- If local guidelines are not available:
 - For an uncomplicated infection, prescribe either:
 - [Trimethoprim](#) 200 mg twice daily, for 3 days, *or*
 - [Nitrofurantoin](#) 50 mg four times daily, or 100 mg (modified-release) twice daily, for 3 days.
 - For a [complicated](#) infection, prescribe a 5–10-day course of trimethoprim or nitrofurantoin.

Basis for recommendation

Antibiotic treatment

- For women with urinary tract infection (UTI), there is [evidence](#) from a meta-analysis that antibiotics are more effective than placebo in eradicating bacteriuria and relieving UTI symptoms [[Falagas et al, 2009](#)].

Duration of antibiotic treatment

- A 3-day course of empirical treatment is recommended because there is good [evidence](#) from Cochrane systematic reviews that this achieves symptomatic cure in people with uncomplicated UTI; it is more effective than single-dose treatment and as effective as 5–10-day courses. This is also in line with

recommendations from the Scottish Intercollegiate Guidelines Network (SIGN) [[SIGN, 2006](#)] and international guidelines [[American College of Obstetricians and Gynecologists, 2008](#); [European Association of Urology, 2009](#)].

- For people with a [complicated](#) UTI, a longer course is recommended because there is [evidence](#) from a Cochrane systematic review that a 5–10-day course produced a higher bacteriological cure rate (but more adverse effects) than a 3-day regimen. The Cochrane systematic review concluded that a 5–10-day course may be considered for women in whom eradication of bacteriuria is important.

Route of administration

- The oral route is recommended, even for severe cystitis. A Cochrane systematic review found no [evidence](#) that oral antibiotic treatment is less effective than intravenous antibiotics for treating severe UTIs [[Pohl, 2007](#)].

Antibiotic choice: trimethoprim and nitrofurantoin as first-line options

- Trimethoprim and nitrofurantoin (both narrow spectrum antibiotics) are generally recommended as appropriate first-line antibiotics in the UK [[SIGN, 2006](#); [BNF 57, 2009](#)].
- Narrow spectrum antibiotics are preferred over broad spectrum antibiotics such as co-amoxiclav, quinolones, and cephalosporins. This is in line with guidance issued by the Health Protection Agency which recommends avoiding the use of broad spectrum antibiotics when narrow spectrum antibiotics remain effective [[HPA, 2009](#)]. There are concerns that broad spectrum antibiotics increase the risk of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant UTIs. Issues of antibiotic resistance are discussed below.
- Despite their widespread use, there are few comparative trials comparing these two antibiotics. There is [evidence](#) from four trials which found trimethoprim and nitrofurantoin to be equally effective and generally well tolerated.
- The dosages recommended are based on those recommended by the manufacturers of these antibiotics and are in line with doses used in [trials](#) [[Goldshield Pharmaceuticals, 2002a](#); [Goldshield Pharmaceuticals, 2002b](#); [Actavis, 2007](#)].

Bacterial resistance

- There are concerns that resistance to trimethoprim and nitrofurantoin is increasing, yet few data on the resistance patterns have been published.

- [Evidence](#) from older studies indicated trimethoprim resistance to be around 20–30% (although higher levels have been reported for certain parts of the UK) with a lower incidence for nitrofurantoin (less than 20%). However, these data should be treated with caution, because:
 - Most of these studies were performed in the 1990s and resistance patterns may have changed.
 - There are considerable geographic variations in antibiotic resistance pattern.
 - It is difficult to compare results from different studies because of differences in populations (for example hospital or community) and differences in laboratory standards.
 - Rates of clinical resistance to trimethoprim may be less common than expected from rates of resistance in laboratory samples. Statistics from laboratories are likely to be biased by higher proportions of samples from women with resistant infections [[McNulty et al, 2006](#)].
- Consequently, CKS recommends that, where available, local antibiotic guidelines should be followed, taking into account local resistance patterns.

Nitrofurantoin formulations

- Both immediate and modified-release formulations of nitrofurantoin are recommended because CKS found no [evidence](#) to prefer one formulation over another. For further information, see [Dosage](#).

When should I culture the urine of a woman with suspected cystitis?

- Urine microscopy and culture are not routinely required for women with uncomplicated cystitis.
- Send urine for microscopy and culture if any of the following apply:
 - There are risk factors for a [complicated](#) urinary tract infection — for example the woman has recently had urological instrumentation, or is immunocompromised, or has been in hospital recently.
 - Confirmation of the [diagnosis](#) or exclusion of [other conditions](#) is required.
 - The woman has not responded to antibiotic treatment.
 - The woman has recurrent episodes of cystitis and this has not been investigated.
 - When underlying causes of recurrent cystitis and other conditions have been excluded, it is not necessary to routinely culture the urine for further episodes.

Basis for recommendation

These recommendations are in line with Scottish Intercollegiate Guidelines Network guidelines [[SIGN, 2006](#)].

Urine culture

- Urine culture is mainly useful for identifying bacteria and their sensitivity to antibiotics [[SIGN, 2006](#)].
- Urine microscopy and culture are not routinely recommended for women with uncomplicated cystitis because the results are not available for immediate decision-making and, by the time they are available, most women's symptoms will be resolving. Three studies found that, if urine were to be routinely cultured for all women with acute cystitis, the average duration of symptoms would be reduced by between 0.04 and 0.32 days [[SIGN, 2006](#)]. Similar [evidence](#) is provided by a randomized controlled trial that compared different strategies for antibiotic treatment [[Little et al, 2009](#)]. An economic analysis estimated the cost of preventing 1 day of symptoms as £215, and the cost per QALY (quality adjusted life year gained) was £215,000 [[SIGN, 2006](#)].
- Urine culture is recommended for women with a [complicated](#) infection because the risks associated with treatment failure are increased [[SIGN, 2006](#)].

How should I follow up a woman with cystitis?

- Follow up is not routinely required for uncomplicated cystitis, but should be considered for women with a potentially [complicated](#) infection.
- If haematuria was found, follow up to re-test the urine and check that the infection and haematuria have resolved.

Basis for recommendation

This recommendation is pragmatic as CKS found no published evidence on which to base recommendations [[SIGN, 2006](#)].

- Follow up is not routinely required for uncomplicated cystitis as most cases of uncomplicated urinary tract infection resolve in about 4–9 days without antibiotic treatment, and in about 3–8 days with antibiotic treatment — see [Prognosis](#).

When should I refer a woman with acute cystitis?

- If the woman fails to respond to two courses of antibiotics shown by urine culture results to be appropriate treatment, refer for specialist assessment.
- If [urological cancer](#) is suspected (for example haematuria persists after successful treatment of cystitis), refer urgently to a team specializing in the management of urological cancer.

Basis for recommendation

Referral for failure to respond to appropriate antibiotics

- The recommendation to consider referring women who have failed to respond to an appropriate antibiotic (shown by urine culture) is pragmatic, as there is no direct evidence from clinical trials or recommendations in national guidelines.

Urgent referral for urological cancer

- The recommendation to refer women with suspected urological cancer is based on criteria in guidelines from the National Institute for Health and Clinical Excellence [[NICE, 2005b](#)].

How should I manage a woman whose cystitis has failed to respond to antibiotics?

- Continue symptomatic treatment with paracetamol or ibuprofen.
- Check compliance with antibiotic treatment.
- Send a urine sample for culture.
- If symptoms are troublesome, offer a different antibiotic (nitrofurantoin or trimethoprim) while waiting for the culture results — see [Choice of antibiotic](#).
- **If infection is confirmed on culture**, treat with an antibiotic to which the organism is sensitive.
- **If infection is not confirmed on culture**, consider other possible causes for the symptoms — see [Differential diagnosis](#).
- **If cystitis symptoms fail to respond to two courses of antibiotic shown by culture to be appropriate treatment**, refer for specialist assessment.

Basis for recommendation

These recommendations are in line with guidance from the Scottish Intercollegiate Guidelines Network [[SIGN, 2006](#)].

- The recommendation to offer a different antibiotic if symptoms persist is supported by a study of the course of uncomplicated community-acquired urinary tract infection in women [[McNulty et al, 2006](#)]. The study found that, after 5 days of antibiotic treatment, symptoms had resolved in 70% of women infected with an organism sensitive to the antibiotic, and 24% of women with a resistant isolate. The study also found that 50% of those who reconsulted in the first week had a resistant isolate.

[Recurrent cystitis in women who are not pregnant](#)

How should I manage an acute episode of recurrent cystitis?

- Review the diagnosis.
 - Culture the urine to confirm infection and exclude [other causes](#).
 - Refer urgently if [urological cancer](#) is suspected.
- Review the woman's medical and surgical history to assess risk factors for recurrent cystitis such as stones, papillary necrosis, and vesicoureteric reflux — this assessment may require imaging and urological referral.
- Relieve symptoms with [paracetamol](#) or [ibuprofen](#).
- If symptoms are moderate or severe, offer an [antibiotic](#) immediately.
- If symptoms are mild, suggest delaying antibiotic treatment until culture results are available to guide choice of antibiotic.
- Advise on [lifestyle measures](#) such as high-strength cranberry capsules to reduce the risk of recurrent episodes.
- If troublesome cystitis recurs frequently:
 - Consider offering a prescription for a 'stand-by' antibiotic to be used for future episodes.
 - Consider [preventive](#) treatments.
- [Refer](#) or seek specialist advice if these measures are not successful.

Basis for recommendation

Confirming urinary tract infection and excluding other causes

- The recommendation to confirm infection with urine culture, and exclude other causes, is pragmatic.
- The recommendation to refer urgently if cancer is suspected is based on guidelines from the National Institute for Health and Clinical Excellence [[NICE, 2005b](#)].

Treatments

- The basis for recommending symptomatic relief with paracetamol or ibuprofen is discussed in [Managing suspected cystitis](#).
- The basis for offering empirical antibiotic treatment if symptoms are moderate or severe, or delaying treatment if symptoms are mild, is discussed in [Managing suspected cystitis](#).
- The recommendation to consider 'stand-by' antibiotics is based on expert opinion [[Harris et al, 2008](#)].

Lifestyle measures and preventive treatment

- The basis for lifestyle measures and prophylactic treatments is discussed in the sections on [Lifestyle measures](#) and [Preventive treatments](#).

Referral

- The basis for the recommendation to refer the woman if prophylactic measures are unsuccessful is pragmatic.

Which antibiotic should I prescribe for a woman with recurrent cystitis?

- Follow local guidelines when available. Otherwise:
 - For empirical treatment, prescribe either:
 - [Trimethoprim](#) 200 mg twice daily, for 3 days, *or*
 - [Nitrofurantoin](#) 50 mg four times daily, or 100 mg (modified-release) twice daily, for 3 days.
 - If the woman has been treated with trimethoprim recently (up to a year previously), consider prescribing nitrofurantoin instead of trimethoprim.

Basis for recommendation

Choice of antibiotic

- The reasons for preferring trimethoprim and nitrofurantoin as first-line options for treating cystitis are discussed in [Choice of antibiotic](#).

Considering nitrofurantoin when trimethoprim has been used recently

- Nitrofurantoin may be preferable for empirical prescribing when the woman has recently used trimethoprim because there is [evidence](#) that uropathogens are more likely to be resistant to trimethoprim if it has been used recently (up to the past year). The evidence is not clear enough to recommend precise thresholds of exposure.
- Trimethoprim is not preferred when nitrofurantoin has previously been used because there is no [evidence](#) that previous treatment with nitrofurantoin increases the chance that future infections will be resistant organisms. Furthermore, laboratory studies find that nitrofurantoin-resistant *Escherichia coli* reproduce substantially less effectively than nitrofurantoin-sensitive *E. coli* (in other words, nitrofurantoin resistance imposes a high fitness cost on the organism) [[Sandegren et al, 2008](#)].

What lifestyle measures should I advise for preventing cystitis?

Advise women with recurrent cystitis that:

- **Cranberry products reduce the recurrence rate of cystitis**, and are available from shops (but not on the NHS).
 - Cranberry products should not be taken if warfarin is being used.
 - High strength capsules (containing at least 200 mg of cranberry extract) are recommended because:
 - They may be more effective than cranberry drinks, which require a large volume to be drunk to provide the same amount of cranberry extract: 200 mg of cranberry extract is equivalent to about 5000 mg of fresh cranberries.
 - Cranberry capsules may be more acceptable than cranberry juice, which some women find difficult to take regularly because of the bitter taste or the large amount of sugar added to mask the bitterness.
- If cystitis is related to sexual intercourse, options to be considered include:
 - A different contraceptive method, if a diaphragm is being used.
 - Voiding soon after intercourse.
 - Using a lubricant if symptoms could be due to mild trauma rather than infection.

Basis for recommendation

Cranberry extract for preventing cystitis

- There is good [evidence](#) that cranberry products effectively prevent cystitis. A Cochrane systematic review of randomized controlled trials found that cranberry products significantly reduced the incidence of urinary tract infections (UTIs) over 12 months, compared with placebo or control treatments. However, withdrawal rates in the trials were high, which may indicate that many women find taking cranberry products unacceptable in the long term. Also, the benefits of cranberry may be less in elderly women and women with a urinary catheter.
- The optimal dose and form of administration of cranberry products is not established. However, higher doses may be more effective than lower doses [[SIGN, 2006](#)].
- Cranberry products should be avoided by people taking warfarin, as they can potentiate its effects [[CSM, 2003](#); [CSM, 2004](#)].

Recurrent cystitis related to sexual intercourse

- These recommendations are based on expert opinion [[Harris et al, 2008](#)].
- The Scottish Intercollegiate Guidelines Network (SIGN) guidelines explain that because 'there is no conclusive association between lifestyle factors, such as diet, hydration, clothing, toileting activity, and sexual activity, and susceptibility to bacterial UTI in adult, non-pregnant women, there is no evidence to support healthcare professionals giving routine advice about lifestyle factors' [[SIGN, 2006](#)].
- The incidence of UTI may be increased in women who use diaphragms — this may relate to the fit and size of the diaphragm putting pressure on the urethra. The incidence of UTI may also be increased in women who use spermicides, but the use of spermicides with condoms is no longer recommended. For further information, see the sections on [Diaphragm and cap](#), and [Male condom](#) in the CKS topic on [Contraception](#).

When should I offer preventive treatments for recurrent cystitis?

- **Consider offering a prescription for a 'stand-by' antibiotic** to be used for future episodes of cystitis before prescribing prophylactic drug treatment.
- When deciding to offer prophylactic drug treatment, consider the frequency, severity, and impact of recurrent cystitis, and whether referral for urological investigation would be appropriate.
- **For recurrent cystitis associated with sexual intercourse:**
 - Offer trimethoprim 100 mg to be taken within 2 hours of intercourse (off-label use).

- **For recurrent cystitis not associated with sexual intercourse:**
 - Offer a 6-month trial of low-dose continuous antibiotic treatment.
 - Suitable antibiotics are:
 - Trimethoprim 100 mg every night.
 - Nitrofurantoin (immediate-release) 50 mg to 100 mg every night (modified-release nitrofurantoin is not licensed for prophylaxis).
- Treatments that are not recommended include:
 - Methenamine hippurate.
 - Oestrogen products (for post-menopausal women).

Basis for recommendation

'Stand-by' antibiotics as an alternative to preventive antibiotics

- The recommendation to consider 'stand-by' antibiotics is based on expert opinion [[Harris et al, 2008](#)].

Post-coital antibiotics

- There is limited [evidence](#) from a Cochrane systematic review that post-coital antibiotics may be more effective than placebo and as effective as continuous antibiotic treatment in preventing urinary tract infection (UTI) associated with sexual intercourse.
- The recommendation to offer trimethoprim 100 mg is extrapolated from [evidence](#) provided by a small, double-blind, randomized controlled trial that co-trimoxazole 240 mg (containing trimethoprim 40 mg and sulfamethoxazole 200 mg) given within 2 hours of intercourse was more effective than a post-coital placebo [[Stapleton et al, 1990](#)]. Trimethoprim (a narrow spectrum antibiotic) has been found to be as effective as co-trimoxazole in treating UTI and produces fewer adverse effects [[SIGN, 2006](#); [BNF 57, 2009](#); [European Association of Urology, 2009](#)]. The European Association of Urology also recommend that it is reasonable to offer the doses of antibiotics used for nightly prophylaxis for post-coital use [[European Association of Urology, 2009](#)].
- Although another study supported the post-coital use of [ciprofloxacin](#) (a quinolone) [[Melekos et al, 1997](#)], broad spectrum antibiotics are less preferred. This is in line with guidance issued by the Health Protection Agency which recommended avoiding the use of broad spectrum antibiotics when narrow spectrum

antibiotics remain effective [[HPA, 2009](#)]. There are concerns that broad spectrum antibiotics increase the risk of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant UTIs.

Referral before starting continuous antibiotic prophylaxis

- Seeking specialist advice before starting continuous antibiotic prophylaxis is recommended pragmatically to decide whether the woman needs investigation to exclude an underlying cause.

Continuous antibiotic prophylaxis

▪ Effectiveness

- There is weak [evidence](#) from a Cochrane systematic review that continuous antibiotics reduce recurrence of urinary tract infections more than placebo but are associated with more adverse effects [[Albert et al, 2004](#)]. There are limited data showing that antibiotics do not continue to prevent bacteriuria after treatment is stopped.
- Continuous antibiotics have not been directly compared with cranberry products [[SIGN, 2006](#)].

▪ Choice of antibiotic

- There is insufficient direct evidence to prefer any particular antibiotic over another. Trimethoprim and nitrofurantoin are recommended options for prophylaxis of recurrent UTI because:
- Narrow spectrum antibiotics, such as trimethoprim and nitrofurantoin, are generally preferred over broad spectrum antibiotics due to concerns over increasing the risk of *Clostridium difficile*, MRSA, and resistant UTIs [[HPA, 2009](#)].
- Both trimethoprim and immediate-release nitrofurantoin are licensed for the prophylaxis of recurrent UTI [[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2002c](#); [Actavis, 2007](#)]. The modified-release formulation of nitrofurantoin is not licensed [[Goldshield Pharmaceuticals, 2007](#)].

▪ Dosage and duration of treatment

- The dosages are based on those recommended by manufacturers of these antibiotics and in line with the dosages used in trials investigating prophylaxis of recurrent UTIs [[Goldshield Pharmaceuticals, 2002c](#); [Goldshield Pharmaceuticals, 2002b](#); [Albert et al, 2004](#); [Actavis, 2007](#)].
- A 6-month trial is recommended, as this reflects the duration of most trials on prophylactic antibiotics. Information on long-term follow up is lacking.

▪ Bacterial resistance

- There are concerns that resistance to trimethoprim and nitrofurantoin is increasing, but there is little current published [evidence](#) on resistance patterns for trimethoprim and nitrofurantoin (see the evidence section on [Prevalence](#)).
- Consequently, CKS recommends that local antibiotic guidelines should be followed, taking into account local resistance pattern.

Treatments not recommended

- **Methenamine hippurate**

- Methenamine hippurate is not recommended for preventing UTI because there is only weak [evidence](#) from a Cochrane systematic review that treatment may be effective for up to 7 days [[Lee et al, 2007](#)].

- **Oestrogen products (for postmenopausal women)**

- Oestrogen products are not recommended for use as preventive treatment in primary care because there is [evidence](#) from a Cochrane systematic review that oral oestrogens are no more effective than placebo in reducing recurrent UTIs in postmenopausal women, and there is conflicting evidence from two small trials on intravaginal oestrogen [[Perrotta et al, 2008](#)].

How should I follow up a woman with recurrent cystitis?

- If prophylactic antibiotics are prescribed, follow up to review progress after 6 months, or sooner if clinically indicated.
- If haematuria was found, follow up to re-test the urine and check that the infection and haematuria have resolved.

Basis for recommendation

CKS found no recommendations regarding follow up in national guidelines. The recommendation to follow up every 6 months is based on trials of [prophylactic antibiotics](#), most of which followed their participants for 6 months.

When should I refer a woman with recurrent cystitis?

- Refer urgently, to a team specializing in the management of urological cancer, if [urological cancer](#) is suspected (for example if haematuria persists after successful treatment of acute cystitis).
- Refer the woman if:

- o Risk factors for recurrent cystitis (such as urinary tract abnormalities, stones, vesicoureteric reflux, papillary necrosis) are present or suspected.
- o There is any known abnormality on ultrasound of kidneys, ureters, and bladder.
- o The response to preventive treatments and lifestyle measures is ineffective.

Basis for recommendation

These recommendations are in line with guidelines issued by the Scottish Intercollegiate Guidelines Network (SIGN) and are based on expert opinion [[SIGN, 2006](#)]. Given the evidence supporting the use of [prophylactic antibiotics](#) and [cranberry products](#), SIGN recommends that these strategies should be explored before referring the woman for specialist investigation.

Urgent referral for urological cancer

- The recommendation to refer women with suspected urological cancer is based on criteria in guidelines from the National Institute for Health and Clinical Excellence (NICE) [[NICE, 2005b](#)].

Referral for assessment of risk factors for recurrent cystitis

- The recommendation to refer for specialist assessment of risk factors for recurrent cystitis is based on expert opinion [[Harris et al, 2008](#)].

Poor response to preventive measures

- The recommendation to seek specialist opinion when preventive measures have failed is pragmatic.

Pregnant and with asymptomatic bacteriuria or cystitis

How should I screen for and manage asymptomatic bacteriuria during pregnancy?

- **Screen for asymptomatic bacteriuria** on the first antenatal visit by sending urine for culture. If asymptomatic bacteriuria is found, send a second urine sample for culture.
- **If the second urine culture confirms asymptomatic bacteriuria**, treat for 7 days with an antibiotic to which the organism is sensitive.
- o Preferred options when sensitivities are known are (in order of preference):
- o [Amoxicillin](#): 250 mg three times daily, for 7 days.

- [Nitrofurantoin](#): 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
- [Trimethoprim](#): 200 mg twice daily, for 7 days (unless the woman is [folate deficient or taking a folate antagonist](#)).
- [Cefalexin](#) (500 mg twice daily, or 250 mg 6-hourly, for 7 days) may be used but is less preferred.
- After treatment, send urine for culture to screen for asymptomatic bacteriuria at every antenatal visit until delivery.
- **If a group B streptococcus is isolated**, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

Basis for recommendation

Screening for asymptomatic bacteriuria

- Guidelines from the National Institute for Health and Clinical Excellence (NICE) on antenatal care recommend that 'Women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy' [[NICE, 2008a](#)]. Guidelines from the Scottish Intercollegiate Guidelines Network (SIGN) are clearer: 'Women who do not have bacteriuria in the first trimester should not have repeat urine cultures' [[SIGN, 2006](#)].
- Culture of urine is recommended rather than dipstick (reagent strip) tests because there is good [evidence](#) that dipstick tests are insufficiently sensitive (in whatever combination) to be used for screening. Urine culture is regarded as the gold standard and is assumed to have (close to) 100% sensitivity for detecting bacteriuria.
- The recommendation that a positive culture be confirmed with a second culture before treating asymptomatic bacteriuria in pregnancy is based on expert opinion [[Nicolle et al, 2005](#); [SIGN, 2006](#)].
- The recommendation to continue to screen for asymptomatic bacteriuria at each subsequent visit after completing antibiotic treatment is consistent with practice in multinational clinical trials, such as that conducted by the World Health Organization's Asymptomatic Bacteriuria Trial Group [[Lumbiganon et al, 2009](#)].

Treating asymptomatic bacteriuria

- Asymptomatic bacteriuria in pregnancy should be treated with an antibiotic because there is consistent [evidence](#) from a Cochrane systematic review that the risk of pyelonephritis is reduced: about seven women need to be treated to prevent one episode of pyelonephritis.

- There is inconsistent evidence that treatment may also reduce the incidence of low birthweight and prematurity.

Choosing antibiotic treatment

- **Where sensitivities are known, amoxicillin is preferred.**
 - The manufacturer of amoxicillin states that its use in pregnancy has been well documented in clinical studies. Unlike nitrofurantoin and trimethoprim, amoxicillin is licensed for the treatment of bacteriuria in pregnancy [[ABPI Medicines Compendium, 2008](#)].
 - Penicillin and cephalosporins are generally the antibiotics of choice for use in pregnancy [[Schaefer et al, 2007](#)].
- **Nitrofurantoin is an alternative if amoxicillin is not suitable.**
 - Nitrofurantoin has been used extensively since the 1950s, and its safety profile in human pregnancy has been well documented [[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2007](#)].
 - There is [evidence](#) from a Cochrane systematic review which supports the use of nitrofurantoin for treating asymptomatic bacteriuria in pregnancy [[Smaill and Vazquez, 2007](#)]. Nitrofurantoin was studied in five of the 14 studies identified (none on trimethoprim). Although significant heterogeneity was present, pooled results from five trials (two used nitrofurantoin) found antibiotics to be more effective than placebo in treating asymptomatic bacteriuria in pregnancy.
 - The efficacy and safety profiles of nitrofurantoin are further supported in a recent large multicentre [study](#) undertaken by the World Health Organization (WHO) in which 778 pregnant women with asymptomatic bacteriuria were treated with nitrofurantoin [[Lumbiganon et al, 2009](#)]. A cure rate of 86% was achieved with a 7-day course.
- **Trimethoprim, used carefully, has a good safety profile during pregnancy.**
 - Concerns have been expressed about the use of trimethoprim during pregnancy because it is a folic acid antagonist, and low levels of folic acid have been associated with serious birth defects.
 - The evidence on the risks of trimethoprim during pregnancy has been critically assessed by the UK Teratology Information Service (UKTIS), formerly the National Teratology Information Service (NTIS) [[NTIS, 2008](#)]. A similar systematic review was conducted by the Centers for Disease Control (CDC) in the USA, to assess the safety of trimethoprim-sulfamethoxazole used for prophylaxis in HIV-infected pregnant women [[Forna et al, 2006](#)]. The NTIS and CDC concluded that the benefits outweighed the risks, which were small. Additionally the NTIS concluded that:

- Trimethoprim should not be used in pregnant women who are folate deficient, or who are taking a folate antagonist (unless they are taking a folate supplement).
- In women with normal folate status, who are well nourished, use of trimethoprim for a short period is unlikely to induce folate deficiency.
- For further information, see [Pregnancy and breastfeeding](#) with trimethoprim.
- **Cefalexin is less preferred** because:
 - Although cefalexin can be used in pregnancy [[Schaefer et al, 2007](#)], the Health Protection Agency recommends avoiding the use of broad spectrum antibiotics (such as co-amoxiclav, cephalosporins, and quinolones) when narrow spectrum antibiotics remain effective [[HPA, 2009](#)]. There are concerns that broad spectrum antibiotics increase the risk of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant UTIs.
- **Duration of antibiotic treatment**
 - The use of a 7-day course is supported by [evidence](#) from a recent WHO study which found that a 1-day course of nitrofurantoin is less effective than a 7-day course for treating asymptomatic bacteriuria in pregnant women (n = 778) [[Lumbiganon et al, 2009](#)].
- **Antibiotic dosages**
 - These are in line with dosages recommended by the manufacturers of these antibiotics.

Managing incidentally-found group B streptococcus infection

- The antenatal care service should be informed when a group B streptococcus (GBS), *Streptococcus agalactiae*, is isolated in urine. GBS bacteriuria, even if treated, may be associated with increased risk of neonatal GBS disease, and so antibiotic prophylaxis should be offered to the woman during delivery. This recommendation is based on expert opinion in guidelines from the Royal College of Obstetricians and Gynaecologists [[RCOG, 2003](#)].

How should I manage a pregnant woman with suspected acute cystitis?

- **Convey a positive approach** and reassure the woman that treatment with an antibiotic will prevent any harm to her baby, and will shorten the duration of symptoms.
- If the woman has fever or loin tenderness, suspect upper urinary tract infection and admit or seek urgent specialist opinion.

- Offer [paracetamol](#) for symptomatic relief. Do not recommend urine alkalinizing agents or cranberry products.
- **Send a urine sample for culture before starting antibiotic treatment.**
- **Prescribe an antibiotic empirically.** If local guidelines are not available, suitable first-line antibiotics are (in order of preference):
 - [Nitrofurantoin](#) 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
 - [Trimethoprim](#) 200 mg twice daily, for 7 days (if the woman is [not folate deficient or taking a folate antagonist](#), and has not been treated with trimethoprim in the past year).
 - [Cefalexin](#) 500 mg twice daily, or 250 mg 6-hourly, for 7 days.
- [Follow up](#) after 48 hours (or according to the clinical situation) to check response to treatment and the urine culture results.
- [Amoxicillin](#) 250 mg three times daily, for 7 days, is recommended only if the organism is reported to be susceptible on the culture results.

Basis for recommendation

Sending urine for culture

- The recommendation to send urine for culture before starting treatment is pragmatic [[SIGN, 2006](#)]. The results can confirm the diagnosis and guide further treatment, especially if the uropathogen turns out to be resistant to the empirically chosen antibiotic.

Relieving symptoms with paracetamol

- The recommendation to relieve symptoms with paracetamol is pragmatic.
- Paracetamol is preferred over ibuprofen because it can be used all stages of pregnancy. For further information, see [Choice in pregnancy or breastfeeding](#) for analgesics and antipyretics.

Treating infection with an antibiotic

- Treatment with an antibiotic is recommended because there is good [evidence](#) from placebo-controlled trials in non-pregnant women with cystitis that antibiotics cure the infection, and experts suggest that urinary tract infection in pregnancy may increase the risk of fetal death, and, in the infant, increase the risks of developmental delay and cerebral palsy [[Foxman, 2002](#); [European Association of Urology, 2009](#)].

- CKS did not recommend that women who have mild symptoms should be offered the option of waiting for the urine culture results before starting antibiotic treatment, although this option is recommended for women who are not pregnant. CKS made no recommendation because no evidence and no published expert opinion was found on this strategy.

Choosing antibiotics for empirical treatment

- The choice of antibiotic for empirical treatment should take into account local rates of resistance in uropathogens, and the safety, tolerability, and cost of antibiotic options [[SIGN, 2006](#)].
- **For empirical treatment, nitrofurantoin is preferred over trimethoprim because:**
 - Nitrofurantoin has been used extensively since the 1950s and its safety profile in human pregnancy has been well documented [[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2007](#)].
 - Although the [evidence](#) on nitrofurantoin for treating symptomatic urinary tract infections (UTIs) in pregnant women is poor (only one small study was identified — none were found on trimethoprim), there is indirect [evidence](#) from a Cochrane systematic review and a large multicentre trial (undertaken by the World Health Organization [WHO], n = 778) supporting its efficacy and safety profiles for asymptomatic bacteriuria in pregnancy. For further information, see [Screening for and managing asymptomatic bacteriuria in pregnancy](#).
 - Although trimethoprim is commonly used to treat symptomatic UTIs, good evidence to support its use in pregnancy is lacking. In addition, a recent survey found that women's dietary intake of iron, vitamin D, calcium, and folate remain below recommended levels [[Ruxton and Derbyshire, 2010](#)].
- **Cefalexin is less preferred** because:
 - Although the safety profile is well documented in pregnancy, the Health Protection Agency recommends avoiding the use of broad spectrum antibiotics (such as cephalosporins) when narrow spectrum antibiotics remain effective [[HPA, 2009](#)].
 - There are concerns that broad spectrum antibiotics increase the risk of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant UTIs.
 - *C. difficile* infection can be life-threatening in pregnant women, and there are case-reports of both maternal deaths and stillborn infants [[Rouphael et al, 2008](#)].
- **Amoxicillin is not recommended for empirical treatment** because:
 - There is [evidence](#) from several urine culture studies that resistance to amoxicillin is higher than for trimethoprim.

Duration of antibiotic treatment

- Evidence on different antibiotic regimens for treating symptomatic UTIs in pregnant women is lacking.
- Given the possible increased risk of fetal complications with a UTI, a 7-day course of antibiotics is preferred over shorter courses. This is extrapolated from indirect evidence which found a higher bacteriological cure with longer antibiotic regimens.
- For women with acute uncomplicated UTI who are not pregnant, a Cochrane systematic review found a 5–10-day course produced a higher bacteriological cure (but more adverse effects) than a 3-day course. The authors concluded that a 5–10 day regimen may be considered for women in whom eradication of bacteriuria is important.
- A recent large WHO [study](#) found a higher cure rate with a 7-day course of nitrofurantoin (86%) than a 1-day regimen (76%) in pregnant women with asymptomatic bacteriuria [[Lumbiganon et al, 2009](#)]. Adverse effects were not statistically different between the two groups.
- A 7-day course is supported by guidance issued by the European Association of Urology (no evidence provided) [[European Association of Urology, 2009](#)].

Following up to ensure eradication of infection

- Following up to ensure eradication of infection is based on expert opinion [[SIGN, 2006](#)].
- Subsequent screening for asymptomatic bacteriuria at antenatal visits is a pragmatic recommendation.

Managing incidentally-found group B streptococcus infection

- The antenatal care service should be informed when a group B streptococcus (GBS), *Streptococcus agalactiae*, is isolated from urine. GBS bacteriuria, even if treated, may be associated with increased risk of neonatal GBS disease, and so antibiotic prophylaxis should be offered to the mother during delivery. This recommendation is based on expert opinion in guidelines from the Royal College of Obstetricians and Gynaecologists [[RCOG, 2003](#)].

How should I follow up a pregnant woman with cystitis?

- Review culture results when available and, if necessary, change to an antibiotic that the organism is sensitive to.
- Send urine cultures to screen for asymptomatic bacteriuria 7 days after completion of treatment, and at every antenatal visit until delivery.

- **If a group B streptococcus is isolated**, inform the antenatal care service, as prophylactic antibiotics may be indicated during labour and delivery.

Basis for recommendation

Following up to ensure eradication of infection

- Following up to ensure eradication of infection is a pragmatic recommendation [[SIGN, 2006](#)].
- Subsequent screening for asymptomatic bacteriuria at antenatal visits is a pragmatic recommendation.

Managing incidentally-found group B streptococcus infection

- The antenatal care service should be informed when a group B streptococcus (GBS), *Streptococcus agalactiae*, is isolated from urine. GBS bacteriuria, even if treated, may be associated with increased risk of neonatal GBS disease, and so antibiotic prophylaxis should be offered to the woman during delivery. This recommendation is based on expert opinion in guidelines from the Royal College of Obstetricians and Gynaecologists [[RCOG, 2003](#)].

When should I refer a pregnant woman with cystitis?

- Admit, or seek urgent specialist opinion, if upper urinary tract infection is suspected (fever, loin tenderness, and pain).
- Seek specialist advice if symptoms fail to respond to antibiotic treatment guided by urine culture results, and if other causes have been excluded — see [Differential diagnosis](#).

Basis for recommendation

Admitting pregnant women with suspected pyelonephritis

- Experts recommend arranging admission for all pregnant women with acute pyelonephritis, for at least a short observation period, because of the risk of preterm labour and maternal renal complications [[Ramakrishnan and Scheid, 2005](#)].

Referring when treatment fails

- The recommendation to refer the woman when treatment fails is pragmatic. CKS found no relevant clinical trials or advice in national guidelines.

How should I manage a pregnant woman whose cystitis has failed to respond to antibiotics?

- Check compliance with antibiotic treatment.
- Continue symptomatic treatment with paracetamol.
- Send a urine sample for culture.
- If symptoms are troublesome, offer a different antibiotic (nitrofurantoin or trimethoprim) while waiting for the culture results — see [Managing suspected acute cystitis during pregnancy](#).
- **If infection is confirmed on culture**, treat with an antibiotic to which the organism is sensitive.
- **If infection is not confirmed on culture**, consider other possible causes for the symptoms — see [Differential diagnosis](#).
- **If cystitis symptoms fail to respond to a second antibiotic shown by urine culture results to be appropriate treatment**, seek specialist advice.

Basis for recommendation

These recommendations are in line with guidance from the Scottish Intercollegiate Guidelines Network [[SIGN, 2006](#)].

- The recommendation to offer a different antibiotic if symptoms persist is supported by a recent study of the course of uncomplicated community-acquired urinary tract infection in women [[McNulty et al, 2006](#)]. The study found that, after 5 days of antibiotic treatment, symptoms had resolved in 70% of women infected with an organism sensitive to the antibiotic, and 24% of women with a resistant isolate. The study also found that 50% of those who reconsulted in the first week had a resistant isolate.

Lower UTI in women with an indwelling catheter

How should I treat lower UTI in a woman with an indwelling catheter?

- **Do not treat asymptomatic bacteriuria.**
- Remember that considerable clinical judgement is required to [diagnose](#) urinary tract infection (UTI) in women with an indwelling urinary catheter.
- If symptoms are severe (for example, severe nausea and vomiting, confusion, tachypnoea, tachycardia, hypotension, reduced urine output), admit to hospital as intravenous antibiotics may be required.

- **Check that the catheter is correctly positioned and not blocked.**
- If the catheter has been in place for more than a week, consider changing it before starting antibiotic treatment.
- If there is fever, or loin pain, or both, manage as upper UTI, see the CKS topic on [Pyelonephritis - acute](#).
- Otherwise, treat for lower UTI:
 - Relieve symptoms with [paracetamol](#) or [ibuprofen](#).
 - **Send urine for culture and microscopy** before starting antibiotic treatment.
 - **Prescribe an antibiotic for 7 days, following local guidelines when available.**
 - If symptoms are mild, consider withholding antibiotics until the result of urine culture is available to guide choice of antibiotic.
 - If symptoms are moderate or severe, [empirically](#) prescribe an antibiotic.
 - **Follow up after 48 hours** (or according to the clinical situation) to check response to treatment and the result of urine culture.

Basis for recommendation

Using clinical judgement to decide when to use antibiotics

- Careful clinical judgement is recommended when deciding to use an antibiotic in a person with an indwelling urinary catheter. This is because all people with a long-term indwelling urinary catheter will have bacteriuria at some stage; there is no good evidence that antibiotics are beneficial; and repeated treatment of asymptomatic bacteriuria increases the risk of colonization by drug-resistant bacteria [[SIGN, 2006](#); [European Association of Urology, 2009](#)].

Admitting to hospital

- The recommendation to admit to hospital if systemic symptoms and signs are present is based on expert opinion [[SIGN, 2006](#)].

Reviewing catheter care

- The recommendation to review the care of the catheter is based on expert opinion [[NICE, 2003](#); [European Association of Urology, 2009](#)].

- The recommendation to consider changing the catheter before starting antibiotic treatment for urinary tract infection is based on [evidence](#) from one small trial and expert opinion [[SIGN, 2006](#); [European Association of Urology, 2009](#)].

Using urine culture to guide the choice of antibiotic

- The recommendation to use urine culture to guide treatment and, if practical, to withhold treatment until culture results are available, is based on expert opinion and is intended to reduce the risks of complications and treatment failure, which are generally increased in people with an indwelling urinary catheter [[SIGN, 2006](#)].
- The recommendation to change to a more appropriate antibiotic if the antibiotic was started empirically and a resistant organism is isolated on urine culture is based on expert opinion; it is intended to reduce the risks of complications and treatment failure [[SIGN, 2006](#); [European Association of Urology, 2009](#)].

Treating for 7 days

- Antibiotic treatment for 7 days is recommended because the [evidence](#) is too weak to recommend shorter courses as equally effective.

Relieving symptoms

- CKS found no trials of analgesics for the symptoms of cystitis. The recommendation to use paracetamol or ibuprofen to treat the symptoms of cystitis is based on their use in other painful infections and the experience of experts [[SIGN, 2006](#)].

Which antibiotic should I prescribe empirically for UTI in a woman with an indwelling urinary catheter?

- Follow local guidelines when available. Otherwise:
 - For empirical treatment, prescribe either:
 - [Trimethoprim](#) 200 mg twice daily, for 7 days, *or*
 - [Nitrofurantoin](#) 50 mg four times daily, or 100 mg (modified-release) twice daily, for 7 days.
 - If the woman has a history of recurrent infections, or has recently (within the past year) taken trimethoprim, do not use trimethoprim for empirical treatment.

Basis for recommendation

Choosing an antibiotic

- As there is no direct [evidence](#) from clinical trials of different antibiotics in women with an indwelling urinary catheter, the recommendation to prescribe trimethoprim or nitrofurantoin for empirical treatment of cystitis is based on the recommendations in [Managing suspected cystitis](#).

Treating for 7 days

- Antibiotic treatment for 7 days is recommended because there is only weak [evidence](#) from one small trial that shorter courses are equally effective for urinary tract infection in people with an indwelling urinary catheter.

How can I prevent urinary tract infections in women with indwelling catheters?

- **Ensure an indwelling urinary catheter is appropriate**
 - Use an indwelling catheter only after alternative methods of management have been considered.
 - Regularly review the clinical need for catheterization and remove the catheter as soon as possible.
 - Use intermittent catheterization in preference to an indwelling catheter if this is clinically appropriate and is a practical option for the person.
- **Prevent the introduction of infection**
 - Healthcare personnel should be trained and assessed in their competence to perform urethral catheterization using aseptic procedures.
 - Urine samples should be obtained from a sampling port using an aseptic technique.
 - Catheters should be changed only when clinically necessary (for example, to prevent blockage), or according to the manufacturer's recommendations.
 - When changing catheters, antibiotic prophylaxis should only be used for people with a history of catheter-associated urinary tract infection following catheter change.
- **Do not use:**
 - Bladder instillations or washouts.
 - Prophylactic antibiotics when changing catheters in women with a heart valve lesion, septal defect, patent ductus, or prosthetic valve.

- o Topical antiseptics or antibiotics applied to the catheter, urethra, or meatus; daily washing of the meatus with soap and water is sufficient.

Basis for recommendation

These recommendations are based on guidelines from the National Institute for Health and Clinical Excellence (NICE) [[NICE, 2003](#)].

Minimizing the use of indwelling urinary catheters

- The recommendations on training and practical ways to minimize the use of indwelling urinary catheters reflect guidelines from NICE [[NICE, 2003](#)].
- NICE based their recommendation to use intermittent catheterization rather than an indwelling urinary catheter on a systematic review which included 22 studies and 10 further studies.

Not using bladder instillations or washouts

- Bladder instillations and washouts are discouraged because the NICE systematic review found good evidence that they do not prevent urinary tract infections, and there is concern that they may have local toxic effects [[NICE, 2003](#)].

Not using prophylactic antibiotics or antiseptics

- The recommendation not to use prophylactic antibiotics when changing catheters is based on findings from two studies in the NICE systematic review that not using antibiotic prophylaxis did not increase the risk of urinary tract infection [[NICE, 2003](#)].
- The recommendation not to use prophylactic antibiotics when changing catheters in women with a heart valve lesion, septal defect, patent ductus, or prosthetic valve is based on the NICE clinical guideline on prophylaxis for infective endocarditis, which found this not to be cost-effective [[NICE, 2008b](#)].
- The recommendation not to use topical antiseptics or antibiotics applied to the catheter, urethra, or meatus is based in findings from six clinical studies that compared meatal cleansing with a variety of antiseptic/antimicrobial agents or soap and water; use of antiseptics and antimicrobial agents did not reduce the rate of bacteriuria [[NICE, 2003](#)].

How should I follow up a woman with an indwelling catheter and treated for UTI?

- Review after 48 hours, or according to the clinical situation, to ensure the woman is responding to treatment, and to check the results of the urine culture.
- If urine culture shows that the organism is resistant to the current antibiotic, and:
 - If symptoms have not resolved, change to an antibiotic that the organism is sensitive to.
 - If symptoms have resolved, consider continuing with the current antibiotic.
 - If symptoms recur, start treat with an antibiotic shown in the culture to cover the infecting organism.
- If the woman fails to respond to two courses of antibiotic shown by urine culture to be appropriate treatment, and compliance has been checked, consider referring for assessment and investigation.

Basis for recommendation

These recommendations are pragmatic. CKS found no published expert opinion.

- When the uropathogen is resistant to the empirically chosen antibiotic and the woman has responded, the recommendation to consider continuing treatment until the end of the antibiotic course is based on comments of expert reviewers of previous versions of CKS topics on urinary tract infection. If symptoms have resolved, there is likely to be little added benefit from changing the antibiotic, because, either the woman is getting better of their own accord, or the laboratory assessment of resistance does not reflect the true susceptibility of the uropathogen.

When should I refer a woman with an indwelling catheter and treated for UTI?

- Consider referring for assessment and investigation if the woman fails to respond to two courses of antibiotic shown by urine culture to be appropriate treatment, and compliance has been verified.
- If [urological cancer](#) is suspected (for example if haematuria persists after successful treatment of cystitis), refer urgently to a team specializing in the management of urological cancer.

Basis for recommendation

Referral for failure to respond to appropriate antibiotics

- The recommendation to consider referring women who have failed to respond to an appropriate antibiotic (shown by urine culture) is pragmatic, as CKS found no direct evidence from clinical trials or recommendations in national guidelines.

Urgent referral for urological cancer

- The recommendation to refer women with suspected urological cancer is based on criteria in guidelines from the National Institute for Health and Clinical Excellence (NICE) [[NICE, 2005b](#)].

Urinary tract infection (lower) - women - Management

Prescribing information

Important aspects of prescribing information relevant to primary healthcare are covered in this section specifically for the drugs recommended in this CKS topic. For further information on contraindications, cautions, drug interactions, and adverse effects, see the electronic Medicines Compendium (eMC) (<http://emc.medicines.org.uk>), or the British National Formulary (BNF) (www.bnf.org).

Analgesic/antipyretic

What issues should I consider when prescribing paracetamol?

- Paracetamol is well tolerated and rarely causes adverse effects when used at the recommended daily dose [[Aronson, 2006b](#)].
- For women who are pregnant or breastfeeding, paracetamol is the preferred analgesic as it can be used at any time during pregnancy or breastfeeding [[NTIS, 2004](#); [Schaefer et al, 2007](#)]. For further information, see [Choice in pregnancy or breastfeeding](#).
- In older people, paracetamol is often a safer option than a nonsteroidal anti-inflammatory drug.
- Paracetamol is best avoided in people with hepatic impairment or alcohol dependence, because the risk of liver damage is increased.

[[Schaefer et al, 2007](#)]

What issues should I consider when prescribing ibuprofen?

- For a detailed discussion of the contraindications, adverse effects, monitoring issues, and interactions of nonsteroidal anti-inflammatory drugs (NSAIDs), see the CKS topic on [NSAIDs - prescribing issues](#).
- Ibuprofen is generally the preferred NSAID because of its lower risk of gastrointestinal adverse effects [[CSM, 2002](#)].
- As with other NSAIDs, ibuprofen may worsen or precipitate gastrointestinal haemorrhage, asthma, hypertension, renal impairment, or cardiac failure. Avoid ibuprofen if there is a history of peptic ulcer.

- For use in women who are pregnant or breastfeeding, see [Choice in pregnancy or breastfeeding](#).
- Ibuprofen and other NSAIDs are known to interact with ciclosporin, lithium, and methotrexate. NSAIDs should be initiated with caution in people taking these drugs. Consider seeking specialist advice.
- For people with epilepsy who are taking an NSAID, it may be best to avoid the concomitant use of a quinolone. For further information, see the section on [Quinolone and an NSAID](#) in the CKS topic on [NSAIDs - prescribing issues](#).

[[Aronson, 2006a](#); [BNF 57, 2009](#)]

Which analgesic and antipyretic treatment is suitable for use during pregnancy or when breastfeeding?

- Paracetamol is the preferred analgesic as it can be used at the usual dosage and at any stage of pregnancy and during breastfeeding.
- If the use of ibuprofen is considered essential, it can be used in pregnant women, but it should not be used beyond 27 weeks of gestation because of the increased risk of constriction of the ductus arteriosus.
 - Constriction is related to gestational age; it is rare before week 27, but its incidence increases with advancing gestational age, to 50–70% at 32 weeks, and up to 100% with exposure from week 34 onwards.
 - The effect appears not to be dose dependent.
 - If use of ibuprofen is unavoidable, fetal circulation should be monitored regularly (once or twice weekly) with Doppler sonography, and medication use should be stopped as soon as signs of ductal constriction appear.
- Ibuprofen can be used in breastfeeding women.
 - Levels of ibuprofen excreted in breast milk are negligible [[Trent Drug Information Services, 2005](#)].
 - Ibuprofen was not detected in breast milk following administration of 800 mg to 1600 mg daily in two small studies. No adverse effects on breastfed children were reported in both studies and also in a prospective study covering 21 mother-child pairs.

[[Schaefer et al, 2007](#)]

Trimethoprim

What dose of trimethoprim should I prescribe?

- **For treatment of urinary tract infection (UTI)**, prescribe trimethoprim 200 mg twice daily.

- For uncomplicated UTIs, treat for 3 days.
- For [complicated](#) UTIs, treat for 5–10 days.
- In pregnant women, treat for 7 days.
- For further information, see [Choice of antibiotic](#), [Screening for and managing asymptomatic bacteriuria in pregnancy](#), and [Managing suspected acute cystitis during pregnancy](#).
- **For long-term prophylaxis**, prescribe 100 mg at night.
- **Reduce the dose if the woman has severe renal impairment** — particularly if treatment is prescribed for more than 3 days (for example, people with [complicated](#) urinary tract infection or for long-term prophylaxis).
- For a glomerular filtration rate (GFR) of 15–25 mL per minute, prescribe the normal dose for 3 days, then reduce the dose by half.
- For a GFR less than 15 mL per minute, prescribe half the normal dose.

Basis for recommendation

Standard dose

- These doses are based on those recommended by the manufacturer of trimethoprim and the British National Formulary [[Actavis, 2007](#); [BNF 57, 2009](#)].

Dose in renal failure

- Dose adjustment is recommended for people with severe renal impairment because of the risk of drug accumulation in these people — 40–60% of the trimethoprim dose (along with its metabolites) is excreted unchanged in the urine within 24 hours [[Actavis, 2007](#)].

What are the contraindications for trimethoprim?

- Avoid using trimethoprim in women with blood dyscrasias.

Basis for recommendation

Because of its potential anti-folate effect, there have been reports that trimethoprim causes blood disorders. For further information, see [Adverse effects](#). Consequently, trimethoprim is contraindicated in people with dyscrasias [[Actavis, 2007](#); [BNF 57, 2009](#)].

What are the precautions for trimethoprim?

Trimethoprim should be prescribed with caution in the following conditions:

- **Severe renal impairment**
 - As the drug is predominantly excreted by the kidney, dose adjustment may be required. For further information, see [Dosage](#).
- **Folate deficiency**
 - Because of its potential anti-folate effect, there is a risk of further exacerbating folate deficiency in people who are folate deficient or who are predisposed to folate deficiency (for example elderly people). Consequently, consider prescribing a folate supplement (if this has not already been prescribed) — particularly if trimethoprim is prescribed long term.
 - The risk of folate deficiency is also increased when trimethoprim is combined with certain drugs. For further information, see [Drug interactions](#).
- **Pregnancy**
 - See [Pregnancy and breastfeeding](#) with trimethoprim.
- **Long-term trimethoprim treatment**
 - Because of the risk of haematological adverse effects (see [Adverse effects](#)), the British National Formulary (BNF) advises these people should be warned to seek immediate medical attention if the person develops signs of blood disorders.
 - Although the manufacturer of trimethoprim recommends regular blood monitoring, the BNF found no practical evidence to support this.

[[Actavis, 2007](#); [BNF 57, 2009](#)]

Can trimethoprim be prescribed to women who are pregnant or breastfeeding?

- **For women who are pregnant:**

- Trimethoprim can be used during pregnancy (although it should not be used first-line when other alternatives are available — for example, amoxicillin, if the bacterial sensitivity is known).
- For information on treating asymptomatic and symptomatic urinary tract infection in pregnancy, see [Screening for and managing asymptomatic bacteriuria in pregnancy](#) and [Managing suspected acute cystitis during pregnancy](#).
- If trimethoprim is recommended for use during the first trimester:
 - Ensure the woman is taking a folic acid supplement.
 - For most women, prescribe folic acid 400 microgram daily.
 - Consider a higher dose (5 mg daily) if the woman is at high risk of neural tube defects (for further information, see the section on [Advice on folic acid](#) in the CKS topic on [Pre-conception - advice and management](#)).
- **For women who are breastfeeding**
 - Trimethoprim can be used in women who are breastfeeding.

Basis for recommendation

These recommendations are based on information from the UK Teratology Information Service (UKTIS), (formerly the National Teratology Information Service [NTIS]), a reference text, and the manufacturers of trimethoprim [[Actavis, 2007](#); [Schaefer et al, 2007](#); [NTIS, 2008](#)].

Safety in pregnancy

- There is no strong evidence to suggest that trimethoprim is teratogenic and it has been used for many years in pregnant women [[Schaefer et al, 2007](#)].
- Concerns have been expressed about the use of trimethoprim during pregnancy because it is a folic acid antagonist, and low levels of folic acid have been associated with serious birth defects.
- The evidence on the risks of trimethoprim during pregnancy has been critically assessed by the UK Teratology Information Service (UKTIS), formerly the National Teratology Information Service (NTIS) [[NTIS, 2008](#)]. A similar systematic review was conducted by the Centers for Disease Control (CDC) in the USA, to assess the safety of trimethoprim-sulfamethoxazole used for prophylaxis in HIV-infected pregnant women [[Forna et al, 2006](#)]. The NTIS and CDC concluded that the benefits outweighed the risks, which were small. Additionally the NTIS concluded that:

- Trimethoprim should not be used in pregnant women who are folate deficient, or who are taking a folate antagonist (unless they are taking a folate supplement).
- In women with normal folate status, who are well nourished, use of trimethoprim for a short period is unlikely to induce folate deficiency.
- Trimethoprim is not licensed for use during pregnancy. This is reflected in the British National Formulary which recommends that it should be avoided in the first trimester due to its anti-folate effect [[BNF 57, 2009](#)].

Folic acid supplement

- When trimethoprim is prescribed during the first trimester, the recommendation to co-prescribe a folic acid supplement is precautionary [[Schaefer et al, 2007](#); [NTIS, 2008](#)].
- The standard folic acid dosage for pregnant women is usually recommended [[Schaefer et al, 2007](#)].
- In the UK, most pregnant women should be covered; folic acid supplementation (400 micrograms per day) is routinely recommended for women who wish to conceive and should be taken up to week 12 of pregnancy to prevent neural tube defects in the fetus. For some women at high risk of neural tube defects, a higher dose (5 mg per day) is recommended. For further information, see the section on [Advice on folic acid](#) in the CKS topic on [Pre-conception - advice and management](#).

Breastfeeding

- Trimethoprim may be used during breastfeeding [[Schaefer et al, 2007](#)].
- Although it is excreted in breast milk, the manufacturer of trimethoprim states that short-term trimethoprim treatment is not contraindicated in women who are breastfeeding [[Actavis, 2007](#)].

What drug interactions should I be aware of with trimethoprim?

The following drug interactions have been reported with trimethoprim, when it is combined:

- **With methotrexate (a folate antagonist):**
 - Several cases of bone marrow suppression have been reported (some fatal) [[Baxter, 2008](#)].
- **With azathioprine:**
 - Increased risk of haematological toxicity has been reported in some people with renal transplant and taking azathioprine — particularly if both drugs are given over a prolonged period [[Baxter, 2008](#)].
 - Nevertheless, for most people, both drugs can be taken together. The combination is commonly used in practice.

- The reaction is also expected for mercaptopurine (a metabolite of azathioprine).
 - **With phenytoin:**
 - There is a small risk of phenytoin toxicity (particularly if the serum phenytoin levels are at the top end of the range) as trimethoprim can decrease the clearance of phenytoin [[Baxter, 2008](#)]. Signs of phenytoin toxicity include blurred vision, nystagmus, ataxia, or drowsiness.
 - This interaction is also expected with fosphenytoin (a pro-drug of phenytoin).
 - **With ciclosporin:**
 - Increased nephrotoxicity has been reported. However, this interaction has not been firmly established [[Baxter, 2008](#)].
 - **With digoxin and warfarin.** However the clinical significance of these interactions is still uncertain [[Baxter, 2008](#)].
 - **Digoxin:** trimethoprim has been reported to increase digoxin levels by an average of 22% in nine elderly people after taking trimethoprim 200 mg daily for 14 days (although an increase of 75% was experienced by one person). Consider monitoring for signs of digoxin toxicity in the elderly if trimethoprim is given long term for prophylaxis [[Baxter, 2008](#)].
 - **Warfarin:** the manufacturer of trimethoprim warns that it may potentiate the anticoagulant effect of warfarin. However, no case reports or controlled trials on this interaction have been reported. Although there is some indication of increased anticoagulant effect from two cohort studies, the interaction is likely to be small (if it occurs), requiring little or no adjustment in warfarin dose [[Baxter, 2008](#)].
- [[Baxter, 2008](#); [BNF 57, 2009](#)]

What adverse effects are associated with trimethoprim?

- Trimethoprim is generally well tolerated.
- Nausea, vomiting, pruritus, and skin rashes have occasionally been reported. These are generally mild and reversible when trimethoprim is withdrawn.
- Severe adverse drug reactions with trimethoprim are rare.
- There have been rare reports of trimethoprim causing haematological adverse effects, including [[Aronson, 2006c](#)]:
- Macrocytic and megaloblastic anaemia: this is more likely in people with pre-existing folate deficiency.

- Agranulocytosis — very rare. In people where leukocytes are monitored regularly, mild leukopenia has been reported in 0.4–10% of people taking trimethoprim or co-trimoxazole (trimethoprim plus sulfamethoxazole).
- Aplastic anaemia, neutropenia, thrombocytopenia, and pancytopenia.
- For people receiving long-term trimethoprim treatment, the British National Formulary advises that they should be warned to seek immediate medical attention if they develop signs of blood disorders such as fever, sore throat, rash, mouth ulcers, purpura, bruising, or bleeding [[BNF 57, 2009](#)].

[[Aronson, 2006c](#); [Actavis, 2007](#)]

Nitrofurantoin

What dose of nitrofurantoin should I prescribe?

- **For treatment of acute urinary tract infection (UTI)**, prescribe nitrofurantoin 50 mg four times daily, or 100 mg (modified-release), twice daily.
 - For uncomplicated UTIs, treat for 3 days.
 - For [complicated](#) UTIs, treat for 5–10 days.
 - In pregnant women, treat for 7 days.
 - For further information on duration of treatment, see [Choice of antibiotic](#), [Screening for and managing asymptomatic bacteriuria in pregnancy](#), and [Managing suspected acute cystitis during pregnancy](#).
- **For long-term prophylaxis**, prescribe 50 mg to 100 mg at night.

Basis for recommendation

These doses are based on those recommended by the manufacturer of nitrofurantoin [[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2002c](#); [Goldshield Pharmaceuticals, 2007](#)].

Which formulation of nitrofurantoin should I prescribe?

- Nitrofurantoin is available in the following oral formulations:
 - Immediate-release tablets and capsules (50 mg and 100 mg).
 - Modified-release capsules (100 mg).
 - Oral suspension (25 mg/5 mL).

- **For treatment of urinary tract infection:**

- Both the immediate-release and modified-release formulations may be considered.
- If compliance is a problem, the modified-release formulation may be preferred with its twice-daily dosage (the other formulations need to be taken four times daily).
- If nausea and vomiting is a concern, a formulation that contains macrocrystalline nitrofurantoin (such as immediate-release capsules) may reduce the likelihood of these adverse effects, but the evidence-base to support this is weak.

- **For long-term prophylaxis of UTIs:**

- Prescribe an immediate-release formulation.
- The modified-release formulation is not licensed for long-term prophylaxis.
- The oral suspension may be considered for people with swallowing difficulties or requiring enteral-tube feeding.

Basis for recommendation

For treatment of urinary tract infections (UTIs):

- CKS identified no strong evidence to prefer one nitrofurantoin formulation over another.
- There is weak [evidence](#) from two small RCTs and one retrospective case series that the macrocrystalline formulation of nitrofurantoin (Macrochantin[®] capsules) causes less nausea than the crystalline formulation (Furadantin[®] tablets) in people with a UTI. However, these results should be interpreted with caution as there are a number of methodological weaknesses with these studies.
- No other studies comparing the modified-release nitrofurantoin formulation (Macrobid[®]) with immediate-release formulations of nitrofurantoin were found.
- Given its twice-daily dosage, the modified-release preparation may be preferred if compliance is problem.

For long-term prophylaxis:

- Unlike the modified-release preparations, the immediate-release formulations are preferred as they are licensed for this indication [[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2002c](#); [Goldshield Pharmaceuticals, 2007](#)].

- Long-term prophylaxis only requires one dose to be taken at night. For further information, see [Preventive treatments](#).

What are the contraindications for nitrofurantoin?

- Avoid prescribing nitrofurantoin to people with creatinine clearance less than 60 mL per minute, or elevated serum creatinine.

[[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2002c](#); [Goldshield Pharmaceuticals, 2007](#)]

What are the precautions for nitrofurantoin?

- **Peripheral neuropathy**

- Nitrofurantoin should be used with caution in people with anaemia, diabetes mellitus, electrolyte imbalance, debilitating conditions, and vitamin B (particularly folate) deficiency since these conditions may enhance the occurrence of peripheral neuropathy.
- The manufacturer of nitrofurantoin advises stopping the drug at the first signs of neural involvement (paraesthesiae).

- **People with a deficiency of glucose-6-phosphate dehydrogenase**

- This is found in 10% of black people and a variable percentage of ethnic groups of Mediterranean, near Eastern, and Asian origin. It is rare in Caucasians.
- Avoid nitrofurantoin in these people as it may cause haemolysis.
- Discontinue nitrofurantoin if there is any sign of haemolysis (which ceases when the drug is withdrawn).

- **If the person develops unexplained pulmonary, hepatotoxic, haematological, or neurologic syndromes**, discontinue treatment with nitrofurantoin.

[[Goldshield Pharmaceuticals, 2002b](#); [Goldshield Pharmaceuticals, 2002c](#); [Goldshield Pharmaceuticals, 2007](#)]

Can nitrofurantoin be prescribed to women who are pregnant or breastfeeding?

- Nitrofurantoin can be used in women who are pregnant or breastfeeding.

- Because it is excreted in milk, avoid breastfeeding during treatment with nitrofurantoin if the newborn is glucose-6-phosphate dehydrogenase deficient.

Basis for recommendation

Safety in pregnancy

- Nitrofurantoin has been used for many years for the prophylaxis and treatment of urinary tract infection and asymptomatic bacteriuria in pregnancy [[NTIS, 2005](#); [Schaefer et al, 2007](#)].
- The drug is concentrated in the urinary tract. Consequently, significant transfer across the placenta does not occur.
- Although it is not licensed for use in pregnancy, the manufacturer of nitrofurantoin reported that the drug has been used extensively clinically since 1952 and its suitability in pregnancy has been well documented [[Goldshield Pharmaceuticals, 2002a](#); [Goldshield Pharmaceuticals, 2002b](#)]. The efficacy and safety profiles of nitrofurantoin are further supported by a recent large multicentre [study](#) undertaken by the World Health Organization (WHO) in which 778 pregnant women with asymptomatic bacteriuria were treated with nitrofurantoin [[Lumbiganon et al, 2009](#)].
- There have been no reports of increased risk of congenital malformations [[Schaefer et al, 2007](#)].
- Haemolytic reactions are rare. There has been one case report of haemolytic anaemia in a newborn baby (with glucose-6-phosphate dehydrogenase deficiency) after *in utero* exposure to nitrofurantoin [[Bruel et al, 2000](#); [Schaefer et al, 2007](#)].

Breastfeeding

- Nitrofurantoin may be used in women who are breastfeeding [[Schaefer et al, 2007](#)].
- Because it is excreted in milk, there is a potential to cause haemolytic anaemia in newborns who are glucose-6-phosphate dehydrogenase deficient. However, this is rare, and only one case report has been documented [[Schaefer et al, 2007](#)]. The recommendation to temporarily cease breastfeeding is pragmatic advice.

What drug interactions should I be aware of with nitrofurantoin?

- The use of alkalinizing agents (such as potassium citrate) should be avoided in people taking nitrofurantoin. The antibacterial activity of the nitrofurantoin is reduced when the pH of the urine is increased [[SIGN, 2006](#)].

- Although the manufacturer of nitrofurantoin advises against concomitant administration of magnesium trisilicate with nitrofurantoin (due to reduced absorption), the clinical significance is uncertain as only one very small study in 6 people has reported this effect [[Baxter, 2008](#)].

What adverse effects are associated with nitrofurantoin?

Adverse effects associated with nitrofurantoin

- **Pulmonary:** nitrofurantoin-associated pulmonary reactions are reported in less than 1% of people treated with nitrofurantoin. Common manifestations are dry cough, chest pain, dyspnoea, and hypoxemia. Skin rash, arthralgia, and elevated liver enzymes are occasionally present. Chest imaging shows patchy infiltrates and fibrosis. Treatment includes stopping the medication and prescribing a course of corticosteroids [[Vahid and Wildemore, 2006](#)].
- **Gastrointestinal:** nausea and anorexia have been reported. Vomiting, abdominal pain, and diarrhoea are less common gastrointestinal reactions.
- **Peripheral neuropathy** (including optical neuritis), with symptoms of sensory as well as motor involvement, has been reported infrequently.
- Stop treatment at the first sign of neurological involvement.

Prescribing information on amoxicillin

What are the prescribing issues for amoxicillin?

Dosage

- For adults: prescribe amoxicillin 250 mg three times daily, increasing to 500 mg three times daily for more severe infections.
- For the treatment of symptomatic or asymptomatic urinary tract infections in pregnancy, a 7-day course is recommended.
- For further information, see [Screening for and managing asymptomatic bacteriuria in pregnancy](#) and [Managing suspected acute cystitis during pregnancy](#).

Contraindications

- Amoxicillin should not be taken by people who have *true* penicillin allergy. However, gastrointestinal adverse effects alone (such as nausea, vomiting, or diarrhoea) do *not* constitute an allergy to penicillin [[BNF 57, 2009](#)].

Use in pregnancy and breastfeeding

- Amoxicillin can be used in women who are pregnant or breastfeeding [[Schaefer et al, 2007](#); [ABPI Medicines Compendium, 2008](#)].
- Amoxicillin is licensed for the treatment of bacteriuria in pregnancy [[ABPI Medicines Compendium, 2008](#)].

Adverse effects

- Adverse effects that are commonly reported are gastrointestinal (such as nausea, vomiting, and diarrhoea), and skin rash.

Drug interactions

- Contraceptives: antibiotics may cause the combined oral contraceptive pill or patch to fail during the first few weeks of treatment [[Baxter, 2006](#)]. See the sections on [Antibiotics](#) and [Drug interactions](#) in the CKS topic on [Contraception](#) for information on the combined oral contraceptive pill or patch.
- Advise women to use additional contraception during the course of treatment and for 7 days afterwards. If this 7-day period runs beyond the end of the pack of contraceptive pills, advise the woman to start a new pack without a break (omitting any inactive tablets) [[FFPRHC, 2005](#); [FFPRHC, 2007](#)].
- Anticoagulants: documented reports of oral anticoagulant/penicillin (including amoxicillin) interaction are relatively rare [[Baxter, 2006](#)]. However, the British National Formulary advises that common experience in anticoagulant clinics is that a course of broad spectrum penicillin can alter the international normalized ratio [[BNF 57, 2009](#)].

[[ABPI Medicines Compendium, 2008](#); [BNF 57, 2009](#)]

Cefalexin

What are the prescribing issues for cefalexin?

Cefalexin is a first generation cephalosporin.

Dosage

- For uncomplicated urinary tract infections: prescribe cefalexin 250 mg every 6 hours, or 500 mg every 12 hours.
- For treatment of symptomatic or asymptomatic urinary tract infections (UTIs) in pregnancy, a 7-day course is recommended.
- For further information, see [Screening for and managing asymptomatic bacteriuria in pregnancy](#) and [Managing suspected acute cystitis during pregnancy](#).

Contraindications and precautions

- Cefalexin should not be taken by people with known allergy to the cephalosporin group of antibiotics.
- Cephalosporins should be given cautiously to penicillin-sensitive people. The British National Formulary advises that about 10% of penicillin-sensitive people will also be allergic to cephalosporins [[BNF 57, 2009](#)].
- The Health Protection Agency advises that broad spectrum antibiotics (such as co-amoxiclav, quinolones, and cephalosporins) should be avoided when narrow spectrum antibiotics remain effective, as they increase risk of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and resistant UTIs [[HPA, 2009](#)].

Use in pregnancy and breastfeeding

- Although cefalexin is not licensed in these groups, the manufacturer reported no evidence of teratogenicity in clinical studies [[ABPI Medicines Compendium, 2005](#)].
- Cephalosporins (such as cefalexin) can be used in women who are pregnant or breastfeeding [[Schaefer et al, 2007](#)].

Adverse effects

- Gastrointestinal adverse effects (such as nausea, vomiting, and diarrhoea), are commonly reported.
- The manufacturer of cefalexin advises that pseudomembranous colitis should be considered in people who develop antibiotic-associated diarrhoea [[ABPI Medicines Compendium, 2005](#)]. It can be mild, or can be life threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone.

Drug interactions

- Contraceptives: antibiotics may cause the combined oral contraceptive pill or patch to fail during the first few weeks of treatment [[Baxter, 2006](#)] (see the sections on [Antibiotics](#) and [Drug interactions](#) in the CKS topic on [Contraception](#) for information on the combined oral contraceptive pill or patch):

- Advise women to use additional contraception during the course of treatment and for 7 days afterwards. If this 7-day period runs beyond the end of the pack of contraceptive pills, advise the woman to start a new pack without a break (omitting any inactive tablets) [[FFPRHC, 2005](#); [FFPRHC, 2007](#)].
- Anticoagulants: documented reports of oral anticoagulant/penicillin (including amoxicillin) interaction are relatively rare [[Baxter, 2006](#)]. However, the British National Formulary advises that common experience in anticoagulant clinics is that a course of broad spectrum penicillin can alter the international normalized ratio [[BNF 57, 2009](#)].

[[ABPI Medicines Compendium, 2005](#); [BNF 57, 2009](#)]