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Who should read this document?

This policy applies to all clinical staff involved the prescribing of antimicrobials.

Key Practice Points

Treatment of a UTI should normally be reserved for symptomatic patients. See Treatment algorithm for further details on when to start or withhold antibiotics.

Duration of treatment will depend on whether or not the infection is simple or complicated, so the patient must be assessed for factors which would suggest a complicated UTI.

This policy includes empiric treatment regimes for Urinary tract infections, including sepsis due to UTI, UTI in pregnancy, Prostatitis and Epididymo-orchitis.

Background/ Scope/ Definitions

Antimicrobial agents are among the most commonly prescribed drugs and account for 20% of the hospital pharmacy budget. Unfortunately, the benefits of antibiotics to individual patients are compromised by the development of bacterial drug resistance. Resistance is a natural and inevitable result of exposing bacteria to antimicrobials.

Good antimicrobial prescribing will help to reduce the rate at which antibiotic resistance emerges and spreads. It will also minimise the many side effects associated with antibiotic prescribing, such as Clostridium difficile infection. It should be borne in mind that antibiotics are not needed for simple coughs and colds. In some clinical situations, where infection is one of several possibilities and the patient is not showing signs of systemic sepsis, a wait and see approach to antibiotic prescribing is often justified while relevant cultures are performed.

This document provides treatment guidelines for the most common situations in which antibiotic treatment is required. The products and regimens listed here have been selected by the Trust’s Medicines Management Group on the basis of published evidence. Doses assume a weight of 60-80kg with normal renal and hepatic function. Adjustments may be needed for the treatment of some patients.

This document provides treatment guidelines for the appropriate use of antibiotics. The recommendations that follow are for empirical therapy and do not cover all clinical circumstances. Alternative antimicrobial therapy may be needed in up to 20% of cases. Alternative recommendations will be made by the microbiologist in consultation with the clinical team.

This document refers to the treatment of adult patients (unless otherwise stated).
What is new in this version?

Remove 'Indwelling catheter' as a risk factor for complicated UTI as these patients should not be treated with nitrofurantoin for lower UTI but as per algorithm 2.

Replace 'if eGFR <30mL/min or if patient has AKI' with 'if patient has a known or suspected AKI' as our gentamicin dosing guidelines give advice on dosing in patients with CKD and it may be appropriate to use gentamicin in this group.

UTI in pregnancy section updated. New evidence suggests that nitrofurantoin does not need to be avoided in the third trimester any more (see references). Choices brought in line with PHE and local CCG guidance.

Guideline

General principles and Microbiological Sampling

Antimicrobial treatment should be reserved for patients with urinary symptoms (frequency, urgency, dysuria), except for the following two situations:

a) Asymptomatic bacteriuria (>100,000 cfu/ml) in a screening sample taken in pregnancy.
b) Asymptomatic bacteriuria in a screening sample taken prior to urological surgery where mucosal bleeding is likely to occur (e.g. transurethral resection of prostate)

If patient reporting urinary symptoms post TWOC (Trial without catheter), consider inflammation as a possible cause. Send an MSU (Midstream sample of urine) for culture if symptoms are suggestive of a urinary tract infection before starting antibiotics. Antimicrobial therapy should only be initiated if there are signs of urinary sepsis.

Microbiological Sampling

While laboratory results are useful for supporting a clinical diagnosis of UTI and for guiding therapy through susceptibility results, they should not be used in place of clinical criteria for diagnosing UTI.

Midstream samples of urine (MSU) culture reports with a mixed growth of bacteria often reflect contamination and sensitivity tests are usually not done or reported. A repeat MSU should be sent if still clinically indicated. A single organism with a count of 100,000 cfu/ml, sometimes known as ‘significant bacteriuria’, has only an 80% probability of being reproducible in a second sample in a clean, voided sample in women with cystitis.

Blood cultures should be taken in serious systemic infection where two or more markers of systemic inflammatory response syndrome are present.
Algorithm 1: Management of possible UTI in uncatheterised patients (excluding pregnant patients)

NB: ‘Cloudy’, ‘smelly’ urine and incontinence are NOT indications for antibiotics or requesting an MSU.

≤2 symptoms suggestive of a UTI (Frequency, dysuria, urgency, suprapubic tenderness)

≥3 symptoms suggestive of a UTI (Frequency, dysuria, urgency, suprapubic tenderness)

Patient has symptoms suggestive of an Upper UTI
- Loin or back pain
- Fever

Patient have new onset confusion or worsening of pre-existing confusion

≥2 signs of systemic infection?
- Chills, rigors
- Temperature >38.3°C or <36°C
- Tachycardia of greater than 90bpm
- Tachypnoea greater than 20 rpm
- WBC > 12x10⁹/l or < 4x10⁹/l

NO

YES

Review diagnosis and investigate as appropriate

Send MSU for culture and **Treat as per Lower UTI section**

Adjust antibiotic choice according to sensitivity results

Send MSU for culture and treat as per **UpperUTI/Pyelonephritis/Sepsis due to UTI**

or **Severe Sepsis due to UTI** policy as appropriate

Adjust antibiotic choice according to sensitivity

NO

YES

Perform a urine dipstick*

Urinalysis (dipstick) shows presence of leukocyte esterase and/or nitrites *

NO

YES

Look for other sources of infection

No Indication for antibiotics

* Blood and protein should not be used in this context
Algorithm 2: Management of possible UTI in catheterised patients

Do NOT collect 'routine' CSU (Catheter Specimen of Urine) samples from catheterised patients. If done incorrectly this procedure may introduce infection to the urinary tract. CSU samples should only be sent if the urinary tract is a suspected source of the systemic infection.

Symptoms suggestive of a UTI (fever, flank or suprapubic discomfort, change in voiding patterns, nausea, vomiting, malaise or confusion).

Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients.

YES

Send a CSU

All patients with long-term indwelling urinary catheters have bacteriuria and therefore urine dipsticks are not useful in making a diagnosis of catheter associated UTI

NO

Mild symptoms and patient systemically well

Await CSU result and treat accordingly.

Patient systemically unwell

Consider/exclude other sources of infection

Treat as per UpperUTI/Pyelonephritis/Sepsis due to UTI or Severe sepsis due to UTI policy as appropriate

Adjust antibiotic choice according to

Do not treat asymptomatic bacteriuria in catheterised patients.

Patients with a long-term indwelling urinary catheter should normally have their catheter changed when antibiotics are initiated.
<table>
<thead>
<tr>
<th>No Penicillin Allergy</th>
<th>Non-severe Penicillin Allergy</th>
<th>Severe Penicillin Allergy</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1 Lower UTI - Uncomplicated i.e. Non-pregnant female with no risk factors (see ‘Lower UTI – complicated’ below)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin 50mg QDS (contraindicated if eGFR&lt;30ml/min)</td>
<td>Nitrofurantoin 50mg QDS (contraindicated eGFR&lt;30ml/min)</td>
<td>Nitrofurantoin 50mg QDS (contraindicated eGFR&lt;30ml/min)</td>
<td>3 days</td>
</tr>
<tr>
<td>2nd Line or if eGFR&lt;30ml/min Cefalexin 500mg BD</td>
<td>2nd Line or if eGFR&lt;30ml/min Cefalexin 500mg BD</td>
<td><strong>Alternative agents if above cannot be used</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fosfomycin oral 3g stat</td>
<td></td>
</tr>
<tr>
<td><strong>1.2 Lower UTI - Complicated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Risk factors (Male, Diabetes, Renal tract abnormality, Recent urinary surgery, Symptoms &gt;7days, immunosuppressed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• See Prostatitis section below if a male patient has signs or symptoms suggestive of prostatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin 50mg QDS (contraindicated if eGFR&lt;30ml/min)</td>
<td>Nitrofurantoin 50mg QDS (contraindicated eGFR&lt;30ml/min)</td>
<td>Nitrofurantoin 50mg QDS (contraindicated eGFR&lt;30ml/min)</td>
<td>7 days</td>
</tr>
<tr>
<td>2nd Line or if eGFR&lt;30ml/min Cefalexin 500mg BD</td>
<td>2nd Line or if eGFR&lt;30ml/min Cefalexin 500mg BD</td>
<td><strong>Alternative agents if above cannot be used</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fosfomycin oral 3g on alternate days for 3 doses (If eGFR &lt;50mls/min use 3g every 3 days)</td>
<td></td>
</tr>
</tbody>
</table>
### 2 Upper UTI/Pyelonephritis or Sepsis due to UTI

**In AKI (Acute Kidney Injury), dose piperacillin/tazobactam and meropenem as per baseline eGFR for the first 48 hours and then review.**

<table>
<thead>
<tr>
<th>No Penicillin Allergy</th>
<th>Non-severe Penicillin Allergy</th>
<th>Severe Penicillin Allergy</th>
<th>Duration</th>
</tr>
</thead>
</table>
| **1st line:**  
Gentamicin IV*  

* The decision to administer IV gentamicin to a patient with a known or suspected Acute Kidney Injury (AKI) should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered.  

**2nd line if gentamicin cannot be given:**  
Piperacillin/Tazobactam 4.5g TDS**  
(dose reduction required in CKD)  

**Oral Step Down**  
According to sensitivities  

**No sensitivities**  
Cefalexin 500mg BD  

**2nd Line**  
Ciprofloxacin 500mg BD (Specialty consultant or microbiology recommendation)  

If significant urological history and no sensitivities  
Co-amoxiclav 625mg TDS | **1st line:**  
Gentamicin IV*  

* The decision to administer IV gentamicin to a patient with a known or suspected Acute Kidney Injury (AKI) should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered.  

**2nd line if gentamicin cannot be given:**  
Meropenem 1g TDS**  
(dose reduction required in CKD)  

**Oral Step Down**  
According to sensitivities  

**No sensitivities**  
Cefalexin 500mg BD  

**2nd Line**  
Ciprofloxacin 500mg BD (Specialty consultant or microbiology recommendation) | **1st line:**  
Gentamicin IV*  

* The decision to administer IV gentamicin to a patient with a known or suspected Acute Kidney Injury (AKI) should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered.  

**2nd line if gentamicin cannot be given:**  
Ciprofloxacin oral 500mg BD  

**Oral Step Down**  
According to sensitivities  

**No sensitivities**  
Ciprofloxacin 500mg BD (Specialty consultant or microbiology recommendation) | 10 days  
If the patient is failing to respond to gentamicin monotherapy, treat as per ‘Severe sepsis due to UTI’ below
(Consultant urologist/microbiology recommendation)
### 3 Severe sepsis due to UTI

**Criteria for severe sepsis due to UTI**
If patient has 2 or more of the following *with organ dysfunction, hypoperfusion or hypotension (SBP<90)*:
- Temperature > 38°C or < 36°C
- Heart rate > 90 bpm
- Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg (< 4.3 kPa)
- WBC > 12x10^9/l or < 4x10^9/l

**In AKI, dose piperacillin/tazobactam and meropenem as per baseline eGFR for the first 48 hours and then review.**

<table>
<thead>
<tr>
<th>No Penicillin Allergy</th>
<th>Non-severe Penicillin Allergy</th>
<th>Severe Penicillin Allergy</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial treatment</strong></td>
<td>Gentamicin IV* plus Meropenem 1g TDS** (dose reduction required in CKD)</td>
<td>Gentamicin IV* plus Ciprofloxacin oral 500mg BD (IV 400mg BD if NBM)</td>
<td>10 days</td>
</tr>
<tr>
<td>Single dose of Gentamicin IV* plus Piperacillin/Tazobactam 4.5g IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* The decision to administer IV gentamicin to a patient with a known or suspected Acute Kidney Injury (AKI) should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered.</td>
<td>* The decision to administer IV gentamicin to a patient with a known or suspected Acute Kidney Injury (AKI) should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IV continuation treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Fluid responsive and urine is still the likely source of infection Gentamicin IV* plus Amoxicillin 1g IV TDS</td>
<td>Gentamicin IV* plus Ciprofloxacin oral 500mg BD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd line if gentamicin cannot be given: Omit Gentamicin IV</td>
<td>2nd line if gentamicin cannot be given: Ciprofloxacin oral 500mg BD (IV 400mg BD if NBM) Plus Fosfomycin IV 8g BD (Continuation of fosfomycin requires microbiology approval)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**b. Septic shock**  
*Gentamicin IV*  
plus  
Piperacillin/Tazobactam 4.5g IV  
TDS**  
*(dose reduction required in CKD)*

2\(^{nd}\) line if gentamicin cannot be given:  
Piperacillin/Tazobactam 4.5g TDS**  
*(dose reduction required in CKD)*

Oral step down as above

<table>
<thead>
<tr>
<th>4 UTI in Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Treatment should be offered for symptomatic and asymptomatic bacteriuria</td>
</tr>
<tr>
<td>• A urine sample should be sent before commencing antibiotics.</td>
</tr>
<tr>
<td>• Avoid trimethoprim if low folate status or on folate antagonist.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No Penicillin Allergy</th>
<th>Non-severe Penicillin Allergy</th>
<th>Severe Penicillin Allergy</th>
<th>Duration</th>
</tr>
</thead>
</table>
| **First Line**  
Nitrofurantoin 50mg QDS (only if Lower UTI and avoid at term)  
**Second Line**  
Trimethoprim 200mg BD (if sensitivities available)  
*Give folate if 1\(^{st}\) trimester*  
**Third Line**  
Cefalexin 500mg po BD | **First Line**  
Nitrofurantoin 50mg QDS (only if Lower UTI and avoid at term)  
**Second Line**  
Trimethoprim 200mg BD (if sensitivities available)  
*Give folate if 1\(^{st}\) trimester*  
**Third Line**  
Cefalexin 500mg po BD | **First Line**  
Nitrofurantoin 50mg QDS (only if Lower UTI and avoid at term)  
**Second Line**  
Trimethoprim 200mg BD (if sensitivities available)  
*Give folate if 1st trimester*  
**Third Line**  
Cefalexin 500mg po BD | 7 days |

Oral step down as above
If no oral/enteral route or severe sepsis
Ceftriaxone 2g IV OD

If no oral/enteral route or severe sepsis
Ceftriaxone 2g IV OD

Discuss with microbiology
5 MRSA infection of the urinary tract

Treat according to sensitivity results and the above principles. Nitrofurantoin and trimethoprim are active against most isolates. MRSA is also usually susceptible to doxycycline; the dosing schedule is 200mg stat then 100mg daily.

6 Recurrent UTI

Prophylactic antibiotics for patients with recurrent UTI should not be initiated without an assessment of the likely benefits and risks. Cases may be discussed on an individual basis with a microbiologist. As an alternative to long-term prophylaxis, it may be helpful to supply an antibiotic course for a patient to initiate as soon as symptoms occur. Susceptibility results should be used to guide the choice of antimicrobial agents.

Persistent UTI should be considered if the same strain of microorganism responsible for the initial infection is still present in the urine 2 weeks after completing a course of appropriate treatment. Distinguishing between Persistent and Recurrent UTI’s may be useful as a persistent UTI may require further management, such as more extensive urological evaluation or longer duration of antibiotic therapy.

7 Prostatitis

Symptoms

Suspect acute prostatitis in a man who presents with:

- A feverish illness of sudden onset.
- Irritative urinary voiding symptoms (dysuria, frequency, urgency) or acute urinary retention.
- Perineal or suprapubic pain (low back pain, pain on ejaculation, and pain during bowel movements can also occur).
- Exquisitely tender prostate on rectal examination.
- Urine dipstick test suggesting that there are white blood cells and bacteria in the urine.

Diagnosis

MSU for dipstick testing, CSU and blood cultures for bacteria and antibiotic sensitivity

*Do not collect prostatic secretions as prostatic massage could lead to septicaemia or a prostatic abscess, may be very painful, and is not needed for the diagnosis.*

Differential Diagnosis

Exclude conditions with similar presentations, including

- Prostatic abscess — if prostate is fluctuant on gentle palpation.
• Chronic prostatitis — if symptoms present for several weeks or months.
• Cystitis, urethritis, or upper UTI — if no symptoms suggesting that the prostate is affected.
• Acute unilateral or bilateral epididymo-orchitis — if scrotum, testis, or epididymides are painful or swollen.
• Local invasion from cancer of the prostate, bladder, or rectum; or a leaking aortic aneurysm.

Treatment options

The following treatment regimens are empiric.

1st line treatment
Ciprofloxacin 500mg orally twice daily

2nd line treatment (in patients unsuitable or allergic to quinolones)
Trimethoprim 200mg po bd orally twice daily
(see Trimethorprim Alert in Appendix 2)

Not to be used if eGFR ≤30mL/min/1.73m2 or if patient has Acute Kidney Injury (AKI).

Reassess choice of antibiotics after 24–48 hours. The antibiotic prescribed may need to be modified once culture and sensitivity results are available.

Duration
Total duration of antibiotics – 28 days

Follow up

Refer to urology if the infection is not responding adequately to treatment — prostatic abscess may need to be excluded or treated.

Following recovery, refer for investigation to exclude structural abnormality of the urinary tract.

Chronic Bacterial Prostatitis

Symptoms
• History of recurrent or relapsing UTI, urethritis or epidydimitis
• Pain in the perineum or pelvic floor
• Patients frequently reporting genitourinary and pelvic pain/discomfort during a flare up and alleviation of symptoms after antibiotic treatment.
• Patient may be asymptomatic between acute episodes or have mild pelvic pain or irritative voiding symptoms (frequency, urgency).
• Apyrexial, no systemic signs
• Patient may have diffusely tender prostate during acute episodes
Diagnosis

1. Urine dipstick test (for evidence of UTI or other abnormality that may require investigation e.g. haematuria).
2. MSU - urine cultures are sterile unless an acute UTI is present - review past MSU results.
3. Urinary tract imaging to exclude structural abnormalities.

Treatment options

The following treatment regimens are empiric.

1\textsuperscript{st} line treatment
Ciprofloxacin 500mg orally twice daily

2\textsuperscript{nd} line treatment (in patients unsuitable or allergic to quinolones)
Trimethoprim 200mg po bd orally twice daily
(see Trimethoprim Alert in Appendix 2)

Reassess choice of antibiotics after 24–48 hours. The antibiotic prescribed may need to be modified once culture and sensitivity results are available.

Duration

A total treatment period of 4-6 weeks is recommended.

The antibiotic prescribed may need to be modified if culture and sensitivities are available.

Follow up

Repeat MSU after completing treatment – as patients are at risk of relapse

For recurrent UTI, after 28 days of treatment discuss with microbiology

8 Epididymo-orchitis

Epididymitis, inflammation of the epididymis, causes pain and swelling which is almost always unilateral and relatively acute in onset. In some cases, the testes are involved in the inflammatory process (epididymo-orchitis).\textsuperscript{5}

In sexually active adolescents and men younger than 35 years of age, the causative organism is likely to be \textit{Chlamydia trachomatis} or \textit{Neisseria gonorrhoeae}

In men 35 years or older and adolescents and men younger than 35 years of age who are not sexually active, the causative organisms are typically enteric organisms found in lower urinary tract infections, such as \textit{Escherichia coli}. 
Note: It is important to take a full sexual history from patients of all ages (see below for further information)

Signs and symptoms
- Tenderness to palpation on the affected side
- Palpable swelling of the epididymis starting with the tail at the lower pole of the testis and spreading towards the head at the upper pole of the testis +/- involvement of the testicle.
- There may also be:
  - urethral discharge
  - secondary hydrocoele
  - erythema and/or oedema of the scrotum on the affected side
  - pyrexia
- Differentiation between epididymo-orchitis and testicular torsion on clinical examination may be difficult and if any doubt exists then urgent surgical exploration is advocated.

Assessment

1. **Have a very low threshold for suspecting and admitting to exclude testicular torsion**, particularly in adolescents and men younger than 30 years of age.

2. **Identify the most likely causative organism based on risk factors.**
   a. Any sexually transmitted infection:
      i. Age less than 35 years.
      ii. More than one sexual partner in the past 12 months.
      iii. Any urethral discharge.
   b. Gonorrhoeal infection:
      i. Previous gonorrhoea infection.
      ii. Known contact of a person with gonorrhoea.
      iii. Purulent urethral discharge.
      iv. Men who have sex with men.
   c. Enteric organisms associated with lower urinary tract infections:
      i. Low risk sexual history.
      ii. Age 35 years or older.
      iii. History of penetrative anal intercourse.
      iv. Recent urological instrumentation or catheterization.

3. Consider other causes, such as mumps orchitis (may be parotid swelling), Behçet's syndrome, tuberculosis, and amiodarone.

Relevant Investigations

- Obtain a mid-steam urine for dipstick, microscopy, and culture
- Test for sexually transmitted infections.
  - Gonorrhoea
  - Chlamydia
  - Consider trichomoniasis, HIV, hepatitis, and syphilis.
- Gram stained urethral smear OR gram stained preparation from a centrifuged sample of first past urine (FPU) - for the diagnosis of urethritis
- Urethral swab for *N. gonorrhoeae* culture AND/OR first past urine OR urethral swab for nucleic acid amplification test (NAAT) for *N. gonorrhoeae*.
- First pass urine or urethral swab for *C. trachomatis* NAAT.

**Treatment Options**

The following treatment regimens are empiric. The antibiotic prescribed may need to be modified once culture and sensitivity results are available.

*For epididymo-orchitis due to any sexually transmitted pathogen*

Ceftriaxone IV 500mg stat

*plus*

Doxycycline oral 100mg bd for 10-14 days

*For epididymo-orchitis most probably due to chlamydia or other non-gonococcal organisms*

In patients where:
- gonorrhoea considered unlikely as microscopy is negative for gram negative intracellular diplococci AND
- no risk factors for gonorrhoea identified

Doxycycline 100mg by mouth bd for 14 days

*For epididymo-orchitis most probably due to enteric organisms:*

Ciprofloxacin 500mg by mouth twice daily for 10 days

If swelling has worsened or has not started to improve within 3 days of commencing antibiotics, reassess, and consider a change of antibiotics according to laboratory results (no causative organism is found in 30–40% of men with epididymitis), or consider urology referral.

**Follow up**

- Further follow up is recommended at 2 weeks to assess compliance with treatment, partner notification, and improvement of symptoms.
- If swelling persists after antibiotic treatment is completed, refer for an urgent outpatient appointment with a urologist to exclude underlying testicular cancer.
- If a UTI is confirmed, refer to a urologist to investigate for an underlying structural abnormality or urinary tract obstruction.
- If an STI is confirmed screen for other STIs
9 Antibiotic prophylaxis for catheter changes

Prophylactic antibiotics are NOT routinely indicated for catheter insertion or changes.

In accordance with NICE guidelines, antibiotic prophylaxis is only recommended for patients with a history of catheter-associated UTI following a catheter change. Prophylaxis may also be considered at the discretion of the specialty consultant for patients within 6 weeks of prosthetic joint or spinal implantation/revision surgery, or for removal/change of catheter post prostate surgery.

IV Gentamicin 1.5mg/kg as a single dose 30 minutes before catheter change
OR
IM Gentamicin 1.5mg/kg as a single dose 1 hour before catheter change

For IM administration, volumes exceeding 3mls, should not be given at the same site.

If patient reporting urinary symptoms post TWOC, consider inflammation as a possible cause. Send an MSU for culture if symptoms are suggestive of a urinary tract infection before starting antibiotics. Antimicrobial therapy should only be initiated if there are signs of urinary sepsis.

Standards

- Document the Indication/rationale for antimicrobial therapy, including clinical criteria relevant to this.
- Review and document the patient’s allergy status
- Ensure the choice of antibiotic complies with the antibiotic guidelines and you have documented any clinical criteria relevant to the choice of agent.
- Document a management plan including a stop or review date.
- Where relevant, consider drainage of pus or surgical debridement/removal of foreign material.

Explanation of terms & Definitions

A TWOC (Trial Without Catheter) is when the urinary catheter is removed from the bladder for a trial period to determine whether the patient can pass urine without it.

A MSU (Midstream sample of urine) is a sample taken from the middle of the stream of urine, that is sent to a laboratory to be tested for evidence of infection.
A CSU (Catheter specimen of urine) is a sample of urine taken directly from a patients catheter, that is sent of to a laboratory to be tested for evidence of infection.

AKI (Acute Kidney Injury) refers to an abrupt decrease in renal function.

### References and Supporting Documents

1. IDSA guidelines for the diagnosis and treatment of asymptomatic bacteriuria, CID 2005; 40:643-54

### Roles and responsibilities

All clinical staff involved in the prescribing of antimicrobials to adhere to this policy including full documentation on EPMAR as detailed.
**Appendix 1**

**Trimethoprim does not require a dose reduction in renal impairment but should not be used if eGFR ≤30mL/min/1.73m2 or if patient has Acute Kidney Injury (AKI).**

Trimethoprim inhibits the renal tubular secretion of creatinine, without causing a change in glomerular filtration rate. The result of this mechanism is a reversible increase in serum creatinine and thus an apparent decrease in the calculated creatinine clearance.

Studies have shown an average increase of 15-35% in serum creatinine in healthy volunteers. This figure is likely to be higher in patients with Chronic Kidney Disease (CKD).

The rise in serum creatinine may be misinterpreted as a deterioration of renal function. If the dose is reduced in response to a perceived impairment of renal function, administration of subtherapeutic dosages with the potential for treatment failure may occur.

Hyperkalaemia may occur after several days’ therapy with trimethoprim. This occurs more commonly in patients with diabetes, renal insufficiency, elderly patients, and in patients taking other medications known to increase potassium e.g. ACE inhibitors, spironolactone. These patient groups should have potassium levels checked a few days after starting therapy.

Rarely, Acute Interstitial Nephritis has been reported to occur with trimethoprim therapy. Classic signs of this, along with a rise of serum creatinine are fever and rash. Eosinophilia and eosinophiluria support the diagnosis but their absence does not rule it out.

If Acute Kidney Injury (AKI) is suspected on trimethoprim or hyperkalaemia develops, stop therapy immediately and consider an alternate agent such as cephalexin.

Acute kidney injury, in adults, is defined when one of the following criteria is met:
- Serum creatinine rises by ≥ 26µmol/L within 48 hours or
- Serum creatinine rises ≥ 1.5 fold from the reference value, which is known or presumed to have occurred within one week, or
- urine output is < 0.5ml/kg/hr for >6 consecutive hours
Appendix 2

Trimethoprim or Co-trimoxazole (Septrin®) + Methotrexate: Never co-prescribe

A potentially fatal interaction between methotrexate and trimethoprim has been identified. This interaction is extremely serious, and a recent fatality has occurred locally. This potentially fatal interaction can occur even with short courses or low doses of trimethoprim.

Bone marrow suppression can occur abruptly, leading to:
- Life threatening infections as the body cannot produce leukocytes in response to invading bacteria and viruses.
- Anaemia due to a lack of red blood cells.
- Spontaneous severe bleeding due to a deficiency of platelets.

Fatalities have occurred

Key Messages for clinicians

- Never prescribe trimethoprim, not even a short course or a low dose, to patients receiving methotrexate.

- Never prescribe Co-trimoxazole (Septrin®), not even a short course or a low dose, to patients receiving methotrexate.

- Double check to make sure methotrexate is not already prescribed in primary or secondary care as this may not flag on regular medication lists.

- All patients who receive methotrexate long term should have a “significant event” long term medication recorded on their EPR.

- Ensure all patients on methotrexate have an NPSA methotrexate booklet or a blue Monitoring Disease Modifying Drugs book.

- Be aware that:
  - Some information sources do not stress the importance of this interaction.
  - Co-trimoxazole (Septrin®) contains trimethoprim.
## Appendix 3

### Antibiotic dosing in Chronic Kidney Disease (CKD)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose in normal renal function</th>
<th>Dose in renal impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>4.5g TDS</td>
<td>eGFR &lt;20mls/min: 4.5g BD</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1g TDS</td>
<td>eGFR &lt;50mls/min: 1g BD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR &lt;10mls/min: 1g OD</td>
</tr>
</tbody>
</table>