North Bristol NHS
NHS Trust

Antimicrobial Guidelines v7.2 2022

These are empirical guidelines – treatment should be reviewed clinically at 48-72 hours with the results of clinical findings, pathology and imaging results, and microbiological cultures. Antimicrobials can then be stopped, switched to oral therapy, changed to a narrow spectrum agent or continued with further review.

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On behalf of the Antimicrobial Sub-Group of the NBT Drugs and Therapeutics Committee

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Contents

INTRODUCTION

This document outlines the antimicrobial guidelines for North Bristol NHS Trust.

The guidelines are designed with the specific objective of reducing to a minimum the use of cephalosporins, fluoroquinolones and co-amoxiclav. These agents have been implicated as risk factors for the acquisition and infection with multidrug resistant bacteria such as MRSA and ESBL producing E.coli and Klebsiella species. In addition, they have been associated with increased risk of infection with Clostridium difficile and C.difficile associated diarrhoea.

The guidelines are based on policies used by other NHS Trusts in England to reduce the risk of these infections as well as data from Scandinavia and The Netherlands where hospital infections due to multi resistant bacteria and C.difficile are much rarer than in English hospitals.

It follows therefore that these recommendations are not always based on national guidelines either published in the British National formulary or by professional societies. In most cases, the guidelines have been developed by infection specialists and the relevant clinical specialities.

The guidelines should not be used in isolation but be cross-referenced with relevant specialty protocols, and also the Trust Infection Control policies, Microbiology User Guide and the Antimicrobial Stewardship and Prescribing Policy.

Suggested treatments apply to adult patients with normal renal function. When the pathogen is isolated, treatment may be changed to a more appropriate antibacterial if necessary. If no bacterium is cultured the antibacterial can be continued or stopped on clinical grounds.

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1.1. Prescribing Information

The inappropriate use of antimicrobials is associated with:

- Increased selection of drug-resistant organisms
- Changes to the normal bowel flora leading to super-infection with organisms such as Clostridium difficile and Candida species.
- Increased risks of drug-related adverse effects
- Increased costs
- Increased length of stay

Policy:

The Trust Antimicrobial Stewardship and Prescribing Policy is located on LINK

The policy provides standards for and informs all staff of their responsibilities in the safe, effective and appropriate prescribing of antimicrobials (antibacterials, antifungals and antivirals) within the Trust. It also provides information on the Trust's Antimicrobial Stewardship management systems and reporting.

The policy must be read in conjunction with these Antimicrobial Guidelines which provide greater detail on prescribing of individual antimicrobials for treatment and prophylaxis purposes and include advice on managing patients with renal impairment and penicillin allergy.

The following is a summary of the Trust Antimicrobial Stewardship and Prescribing Policy:

- Antimicrobial treatment should not be started unless there is clinical or microbiological evidence of infection. If a serious life-threatening infection is suspected then treatment must be commenced urgently in line with current national guidance.
- Empirical antimicrobial prescribing for treatment or surgical prophylaxis must be in accordance with these Antimicrobial Guidelines unless there is a clear clinical reason. The reason for any departure from the empirical guidelines must be clearly documented in the medical notes.
- Antimicrobial treatment must be reviewed within 48-72 hours and a decision based on clinical and microbiological considerations made and clearly documented in the medical notes.
- Patients on parenteral therapy must be reviewed daily and considered for oral step-down within 24 hours of meeting oral switch criteria (see section 1.2) where appropriate.
- The indication for an antimicrobial must be clearly documented on both the patient's medicine chart and in the medical notes.
- A duration or review date must be clearly documented on both the patient's medicine chart and in the medical notes along with the prescriber's name and contact details. Courses of greater than 7 days must be discussed with an Infection Specialist unless in line with the Antimicrobial Guidelines recommendation for duration.
- Antimicrobials on the Trust restricted antimicrobials list (Appendix D) must only be prescribed after consultation with an Infection Specialist unless prescribed according to these Antimicrobial Guidelines.
- All healthcare professionals must query antimicrobial prescriptions that do not meet the standards in this policy or have incomplete information.

1.2. Switching from intravenous to oral therapy

There are a number of advantages for a prompt switch from IV to oral antibiotic therapy, these are:

- Reduction in the likelihood of infected IV lines and hospital acquired bacteraemia
- Patient is more likely to receive antibiotics at the correct time and miss fewer doses
- Potential reduction in the risk of adverse events (errors in preparation are significantly higher with parenteral drugs compared to oral formulations)
- Reduces patient discomfort and enables improved mobility and the possibility of earlier discharge
- Saves nursing time
- Potential reduction in treatment costs

Policy:

- Patients on parenteral therapy must be reviewed daily and considered for oral step-down within 24 hours of meeting oral switch criteria where appropriate. The rationale for continuing with parenteral antimicrobials must be recorded in the notes.
- Parenteral therapy must only be used in patients who are severely unwell, unable to tolerate oral therapy or when oral antimicrobials would not provide adequate coverage or tissue penetration.

Oral switch criteria:

- temperature <38^{o}C for 24 hours and improvement clinically and in blood biomarkers of infection
- patient able to tolerate oral food and fluids
- absence of ongoing or potential problem of absorption
- required antibiotic concentrations can be achieved by oral therapy
- oral formulation or suitable alternative is available

Suggested options for oral step down therapy are listed in the table below.

IV therapy	**oral step down therapy**
amoxicillin	amoxicillin
amoxicillin + gentamicin + metronidazole	co-amoxiclav
azithromycin	azithromycin
clindamycin	clindamycin
co-trimoxazole	co-trimoxazole
co-trimoxazole + metronidazole	co-trimoxazole + metronidazole
ceftriaxone	consult a Medical Microbiologist
flucloxacillin	flucloxacillin
gentamicin	ciprofloxacin, co-trimoxazole or co-amoxiclav (pivmecillinam, nitrofurantoin or trimethoprim may be suitable for a simple UTI)
meropenem	consult a Medical Microbiologist
piperacillin-tazobactam	
vancomycin	

1.3 Recommended Durations of Antibiotics

Failure to specify course lengths can lead to unnecessarily long courses being administered to patients. This inappropriate usage of antimicrobials has adverse consequences which compromise the efficacy of therapy for individuals and the organisation. These include:

- Increased selection of drug-resistant organisms – including CPE, MRSA, VRE and other resistant organisms
- Changes to the normal bowel flora leading to super-infection with organisms such as Clostridium difficile and Candida species
- Increased risks of drug-related adverse effects
- Increased costs
- Increased length of stay

Policy:

- Suggested durations for a range of conditions are detailed in these Antimicrobial Guidelines.
- Prescribers must specify a duration or review date in the medical notes and on the prescription chart when prescribing an antimicrobial.
- Once a “review” date is reached the prescriber must state the intended duration or new review date on the prescription chart and in the medical notes. Nursing staff must not omit a dose for antimicrobials with a “review” date without confirming with a member of the clinical team.
- For antimicrobials with a specified duration (stop date), nurses should not administer antimicrobials beyond this. If there is no duration documented, or the duration has passed, to urgently query with the clinical team before the next dose is given. Pharmacists may cross through the prescription to prevent any more doses being given after confirming with the clinical team or medical notes that this is the intention. The pharmacist must document this action in the medical notes.
- If a pharmacist encounters an antimicrobial prescription without a specified duration or review date they will contact the clinical team to confirm a course length and add this to the prescription. This discussion must be documented in the medical notes, including who it was discussed with and contact details.
- If a member of the clinical team is unavailable, then as a minimum the pharmacist will make an entry in the medical notes requesting a review, as well as asking the nursing team to confirm with the clinical team prior to the next dose being given.
- If there is still no course length after 5 days, the pharmacist should escalate to the Registrar or Consultant responsible for the patient. If this does not resolve the problem, further escalate to the Antimicrobial Pharmacist or Infection Specialists for advice.
- The following conditions are excluded from the above: infective endocarditis, deep bone and/or joint infection, pleural infections, *Clostridium difficile* associated diarrhoea, tuberculosis.

Indication	Length of course
GI	
Peritonitis	5 days
appendicitis	5 days
pancreatitis	Not recommended
diverticulitis	5 days
Biliary tract infection	5 days
Typhoid fever	7-14 days
Gastro enteritis	not usually indicated
Oesophageal rupture	Discuss with a Medical Microbiologist

Antibiotic associated colitis	10 days
Peritoneal dialysis associated peritonitis	14 days
peritonitis in patients with liver cirrhosis	5 days
Prevention of infection in upper GI haemorrhage	5 days
Chest	
CAP high severity	5 days
CAP moderate severity	5 days
CAP low/mild severity	5 days
Acute exacerbation COPD	5 days
Aspiration pneumonia	5 days
HAP	5 days
acute exacerbations of bronchiectasis	14 days
CNS	
Meningitis	7-10 days
Brain abscesses, neurosurgical infections	Discuss with a Medical Microbiologist
Uro-genital	
Uncomplicated UTI	Males: 5 days, females: 3 days
Complicated UTI	5 days
Acute Pyelonephritis	7 days
Epididymo-orchitis	10 days
Prostatitis	28 days
Sepsis	
Sepsis	Depends on source - discuss with a Medical Microbiologist
Neutropenic sepsis	7 days
Skin, soft tissue and bone	
Cellulitis/ erysipelas	5 days
Animal and human bites	5 days
Wound infection following clean surgery	5 days
Wound infection following contaminated surgery	5 days
Perianal infection/abscess	5 days
Cellulitis at a cannula site	5 days
Cellulitis in a current injecting drug user	5 days
Mastitis and breast abscesses	5 days
Diabetes mellitus foot infection	7-14 days

Burn Wound Infection	5 days, 3 days if no pathogen isolated
Limb Abscess	7 days
Necrotising fasciitis	Discuss with a Medical Microbiologist
Prevention of infection during leech therapy	duration of contact
Open fracture	72 hours or until soft tissue closure, whichever is sooner
Septic arthritis	4 weeks in total (5-7 days IV, remainder PO)
Acute Osteomyelitis – not related to prosthetic joints	minimum 6 weeks in total (5-10 days IV, remainder PO);
Orthopaedic infections with metalwork *in situ*	Discuss with a medical microbiologist
Cardiovascular	
Endocarditis	Discuss with a Medical Microbiologist
Obs & Gynae	
Pelvic Inflammatory Disease	14 days
Third or fourth degree perineal tears	5 days
Manual removal of the placenta	5 days
Hysterosalpingitis	7 days
Post op wound infection	5 days

2. TREATMENT GUIDELINES

Suggested treatments are given below. They apply to adult patients with normal renal function. When the pathogen is isolated, treatment may be changed to a more appropriate antibacterial if necessary. If no bacterium is cultured the antibacterial can be continued or stopped on clinical grounds.

2.1 Gastro-intestinal system

Review antibiotics at 48-72 hours. Therapy should be amended once a definite pathogen has been identified.
IV antibiotics can be de-escalated once IV/oral switch criteria are met. Stop antibiotics if infection has been ruled out. Record all decisions in the notes. State the duration and indication on the drug chart.

Peritonitis	amoxicillin 1g TDS IV + metronidazole 500mg TDS IV + gentamicin IV (see section 6.1 for dosing) for 5 days Penicillin allergy: co-trimoxazole 960mg BD IV + metronidazole 500mg IV TDS + gentamicin IV (see section 6.1 for dosing) for 5 days If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist. If there are concerns with the use of gentamicin, please discuss with a medical microbiologist. Do not just omit the gentamicin, an alternative is required. oral step down: co-trimoxazole 960mg BD + metronidazole 400mg TDS
Patients at high risk of emergency laparotomy	Co-trimoxazole 960mg IV BD + metronidazole 500mg IV TDS for 5 days
appendicitis	amoxicillin 1g TDS IV + metronidazole 500mg TDS IV + gentamicin (see section 6.1 for dosing) for 5 days Penicillin allergy: co-trimoxazole IV 960mg BD + metronidazole IV 500mg TDS + gentamicin IV (see Section 6.1. for dosing) oral step down: co-trimoxazole 960mg BD + metronidazole 400mg TDS If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist. If there are concerns with the use of gentamicin, please discuss with a medical microbiologist. Do not just omit the gentamicin, an alternative is required.
pancreatitis	Not recommended. Consult a Medical Microbiologist
diverticulitis	amoxicillin 1g TDS IV + metronidazole 500mg TDS IV + gentamicin IV (see section 6.1 for dosing) for 5 days penicillin allergy: co-trimoxazole 960mg BD IV + metronidazole 500mg IV TDS + gentamicin IV (see section 6.1 for dosing) for 5 days oral step down: co-trimoxazole 960mg BD + metronidazole 400mg TDS If the patient's eGFR is <20ml/min, please discuss with a medical

	microbiologist. If there are concerns with the use of gentamicin, please discuss with a medical microbiologist. Do not just omit the gentamicin, an alternative is required.
Biliary tract infection (cholecystitis/cholangitis)	gentamicin IV (see section 6.1 for dosing) for 5 days oral step down: ciprofloxacin 500mg BD. Provide MHRA patient information leaflet about quinolone side effects If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist.
H pylori eradication	amoxicillin 1g BD PO + metronidazole 400mg BD PO + omeprazole 20mg BD PO for 7 days; or amoxicillin 1g BD PO + clarithromycin 500mg BD PO + omeprazole 20mg BD PO for 7 days or in penicillin allergy clarithromycin 500mg BD PO + metronidazole 400mg BD PO + omeprazole 20mg BD PO for 7 days
Typhoid fever	ceftriaxone 2g BD IV and ciprofloxacin 400mg BD IV/ 750mg BD PO. Provide MHRA patient information leaflet about quinolone side effects Infection acquired from the Indian subcontinent, Middle East and South East Asia may be covered by multiple antibacterial resistant strains Ongoing management should be discussed with an Infectious Diseases Physician or Medical Microbiologist
Gastro enteritis	antibacterials not usually indicated
Oesophageal rupture	Co-trimoxazole 960mg IV BD + metronidazole 500mg IV TDS + fluconazole 400mg IV OD for 5 days
Clostridium difficile associated colitis	See chapter 4.1 (page 33)
Oral candidiasis	Fluconazole 50mg OD PO for 7 days or Nystatin mouthwash 100,000 units QDS for 7 days
Oesophageal candidiasis	Fluconazole 100mg OD PO for 7 days

2.2 Lower Respiratory Tract Infections

2.2.1 Community acquired pneumonia (CAP)

Diagnosis

Pneumonia is typically an acute febrile illness with cough, breathlessness, often productive of sputum and pleurisy in a patient with or without existing chest disease and new shadowing on chest X-ray. Pneumonia is defined as 'community-acquired' if it presents prior to or within 48 hours of admission.

Initial Management - use an ABCDE approach when assessing acutely unwell patients

- Patients should receive appropriate oxygen therapy with monitoring of oxygen saturations as per NBT guidelines
- Patients should be assessed for volume depletion and may require intravenous fluids
- Order bloods (FBC, U&Es, CRP and LFTs)
- Ensure a chest x-ray is performed within 4 hours
- Start antibiotics **within 4 hours** or within 1 hour if sepsis present

Mortality Score

The CURB65 score should be used and **documented in the patient's notes** to assess the severity of pneumonia. Score one point for each and record the score in the notes. Clinical judgment should be used in addition. Patients with sepsis should be treated as for high severity regardless of CURB65 score.

- **C**onfusion (Mental Test Score of 8 or less, new disorientation in person, place or time)
- **U**rea > 7mmol/L
- **R**espiratory rate ≥ 30/min
- **B**lood pressure: SBP < 90mmHg and/or DBP ≤ 60mmHg
- Age ≥ **65** years

Severity	**Management**	**Empirical Antibiotic therapy**
Review antibiotics at 48-72 hours. Therapy should be amended once a definite pathogen has been identified. IV antibiotics can be de-escalated once IV/oral switch criteria are met. Stop antibiotics if infection has been ruled out. Record all decisions in the notes. State the duration and indication on the drug chart. IV antibiotics that continue beyond 72 hours must have a duration in the notes.		
High severity CURB65 score 3-5	Take sputum and blood cultures. Perform legionella and pneumococcal urinary antigen test (use the CAP order set on ICE) For ICU patients see pathway here	amoxicillin 1g TDS IV plus azithromycin 500mg OD IV for 5 days Oral step down: amoxicillin 500mg TDS + azithromycin 500mg OD If macrolides are contraindicated use doxycycline 200mg stat PO then 100mg OD instead of azithromycin If already receiving amoxicillin or penicillin allergy: co-trimoxazole 960mg BD IV plus azithromycin 500mg OD IV for 5 days *If there are risk factors for S. aureus pneumonia such as a history of influenza or chicken pox, add flucloxacillin 2g QDS IV (unless the patient is already receiving co-trimoxazole).* Add gentamicin IV if suspected urinary infection also present
Moderate severity CURB65 score 2	Take sputum and blood cultures. Consider legionella and pneumococcal urinary antigen test (use the CAP order set on ICE)	amoxicillin 500mgTDS PO for 5 days plus azithromycin 500mg OD PO for 3 days If already receiving amoxicillin or penicillin allergy: co-trimoxazole 960mg BD PO for 5 days plus azithromycin 500mg OD PO for 3 days **or** doxycycline (monotherapy) 200mg stat PO then 100mg OD for 5 days total
Low/mild severity CURB65 score 1	Take sputum cultures	Amoxicillin 500mg TDS PO for 5 days If already receiving amoxicillin or penicillin allergy: doxycycline 200mg stat PO then 100mg OD for 5 days in total; or azithromycin 500mg OD for 3 days.

Other investigations

Examination of sputum for *Mycobacterium tuberculosis* should be considered for patients if any of the following are present: upper lobe consolidation, cavities, miliary changes, a persistent productive cough or present for > 3 weeks and unresponsive to standard course of antibiotics, especially if malaise, weight loss or night sweats, or risk factors for tuberculosis (eg. ethnic origin, social deprivation, elderly). If TB is suspected, avoid the use of quinolones or rifampicin.

Failure to Improve

For patients who fail to improve as expected refer to a respiratory physician or Infection Specialist (Medical Microbiology). Common complications of CAP may include parapneumonic effusion, empyema or lung abscess. Failure to respond is not a reason for escalation of therapy without further investigation.

Discharge and follow up

Do not routinely discharge patients with CAP if in the past 24 hours they have had 2 or more of the following: temperature higher than 37.5°C, respiratory rate 24 breaths per minute or more, heart rate over 100 beats per minute, systolic blood pressure 90 mmHg or less, oxygen saturation under 90% on room air, abnormal mental status, inability to eat without assistance.

Explain to patients with CAP that after starting treatment their symptoms should steadily improve, although the rate of improvement will vary with the severity of the pneumonia, and most people can expect that by:

- 1 week: fever should have resolved
- 4 weeks: chest pain and sputum production should have substantially reduced
- 6 weeks: cough and breathlessness should have substantially reduced
- 3 months: most symptoms should have resolved but fatigue may still be present
- 6 months: most people will feel back to normal.

Advise patients with CAP to consult their GP if they feel that their condition is deteriorating or not improving as expected. Clinical review, including an X-ray to confirm resolution, is appropriate for many patients at around 6 weeks, either with their GP or by a hospital physician. It is the responsibility of the hospital team to arrange the follow-up plan with the patient and the GP. At discharge or at follow-up patients should be offered access to information about CAP.

All patients aged >65 years or at risk of invasive pneumococcal disease who are admitted with CAP and who have not previously received pneumococcal vaccine should receive 23-valent pneumococcal polysaccharide vaccine (23-PPV) at convalescence in line with DH guidelines.

Smoking cessation advice should be offered to all patients with CAP who are current smokers.

Annotated BTS CAP Guideline Summary of Recommendations 2015
www.brit-thoracic.org.uk/quality-improvement/guidelines/pneumonia-adults

NICE Guideline (NG138] 2019. Pneumonia (community acquired): antimicrobial prescribing
www.nice.org.uk/guidance/ng138

2.2.2 Acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD)

Acute exacerbations of COPD are characterized by worsening of a previously static situation. Important symptoms include increased sputum purulence, volume, dyspnoea, wheeze, chest tightness or fluid retention. The differential diagnosis includes pneumonia, pneumothorax, heart failure, pulmonary embolism, lung cancer and upper airway obstruction.

Differentiation from pneumonia is based on the absence of new shadowing on the chest X-ray and localizing physical signs in the chest.

Antibiotics are appropriate if there is purulent sputum, increased breathlessness and increased sputum volume.

Severe (including patients on bipap): amoxicillin 1g TDS IV for 5 days.

Oral step down: amoxicillin 500mg TDS

If patient has already received amoxicillin or penicillin allergy: co-trimoxazole 960mg BD IV/PO for 5 days.

Moderate/mild: doxycycline 200mg PO stat then, 100mg OD for 5 days

2.2.3 Community acquired aspiration pneumonia

When patients aspirate gastric contents, they develop aspiration pneumonitis for which antimicrobial chemotherapy is not required. Consider aspiration pneumonia if there is a history of impaired swallowing or vomiting with possible aspiration ≥48hr before. Infection is indicated by change in sputum quality to purulent, mucopurulent fever and new chest X-ray changes.

amoxicillin 1g TDS IV or 500mg PO TDS for 5 days

If penicillin allergic or patient has already received amoxicillin in last 2 weeks:

co-trimoxazole 960mg BD IV/PO for 5 days

2.2.4 Hospital acquired pneumonia (HAP) and aspiration pneumonia

Diagnosis

Pneumonia is typically an acute febrile illness with cough, breathlessness, often productive of sputum and pleurisy in a patient with or without existing chest disease and **new shadowing on chest X-ray**. Pneumonia is defined as 'hospital-acquired' if it presents at any point 3 days after admission or the patient has had a hospital admission within the last 3 months. HAP is over diagnosed clinically, alternative diagnoses which do not require antibiotics should be actively excluded.

Suspect **aspiration pneumonia** if there is a history of impaired swallowing or vomiting with possible aspiration >48hr before. When patients aspirate gastric contents they develop aspiration pneumonitis for which antimicrobials are not required. Aspiration pneumonia should be treated as pneumonia and specific anti-anaerobic cover such as metronidazole is **not** required.

Initial Management - use an ABCDE approach when assessing acutely unwell patients

- Patients should receive appropriate oxygen therapy with monitoring of oxygen saturations as per NBT guidelines. Consider arterial blood gases.
- Check and monitor temperature, respiratory rate, pulse, blood pressure and mental status.
- If the patient has a NEWS of 5 (or 3 in one parameter) as indicated on the Vitals eObs system, start antibiotics within 1 hour and take blood cultures. Otherwise start antibiotics within 4 hours.
- Patients should be assessed for volume depletion and may require intravenous fluids
- Monitor U&Es, CRP, LFTs and FBC
- Ensure a chest x-ray is performed as soon as possible and certainly **within 4 hours**
- Take a sputum culture
- Review the patient's previous cultures and start treatment according to table below
- If severe infection, ventilator associated infection or drug intolerance, discuss with a medical microbiologist

Classification	**Antibiotic therapy**
Early onset ≤5 days after admission and no antibiotics given in last 2 weeks	amoxicillin 1g TDS IV or amoxicillin 500mg TDS PO for 5 days.
Early onset ≤5 days after admission and antibiotics given in last 2 weeks or penicillin allergy	co-trimoxazole 960mg BD IV/PO for 5 days
Late onset >5 days after admission and no antibiotics given in last 2 weeks	co-trimoxazole 960mg BD IV/PO for 5 days
Late onset >5 days after admission and antibiotics given in last 2 weeks	piperacillin/tazobactam 4.5g QDS IV for 5 days. Discuss with a medical microbiologist or respiratory physician at the earliest opportunity Penicillin allergy – discuss with a Medical Microbiologist
Previous infection, or colonised, with *Pseudomonas aeruginosa*	Ceftazidime 2g TDS IV or ciprofloxacin* 750mg BD PO for 5 days depending on severity and confirm sensitivities with a microbiologist. *Provide MHRA patient information leaflet about quinolone side effects
Previous infection, or colonised, with MRSA	Add vancomycin IV for 5-10 days
Review after 48-72 hours. Therapy should be amended once a definite pathogen has been identified. IV antibiotics can be de-escalated once IV/oral switch criteria are met. Stop antibiotics if infection has been ruled out. Record all decisions in the notes. State duration and indication on the drug chart.	

Failure to Improve

For patients who fail to improve as expected refer to a respiratory physician or Infection Specialist (Medical Microbiology). Common complications of CAP may include parapneumonic effusion, empyema or lung abscess.

Discharge and follow up

Do not routinely discharge patients with HAP if in the past 24 hours they have had 2 or more of the following findings: temperature higher than 37.5°C, respiratory rate 24 breaths per minute or more, heart rate over 100 beats per minute, systolic blood pressure 90 mmHg or less, oxygen saturation under 90% on room air, abnormal mental status, inability to eat without assistance.

For patients with hospital onset COVID-19, see section 2.2.5.2

2.2.5 COVID-19

2.2.5.1 Patients admitted due to COVID-19

Patients with suspected COVID-19 on admission should be treated as community acquired pneumonia until diagnostic tests (laboratory based or point of care as determined by Trust guidelines) have confirmed SARS-CoV2 infection.

These guidelines define the use of specific anti-infectives in COVID-19, that is, antibacterials and the antiviral remdesivir. Corticosteroids, the JAK1 and 2 inhibitor baricitinib, and the interleukin-6 inhibitors tocilizumab and sarilumab have a role in the treatment of COVID-19 – for further information see the NBT guideline for the diagnosis and management of acute COVID-19, available on LINK.

A) Antibacterials

Antibacterials do not have a use in treating COVID-19 and should only be used if there is a strong suspicion of bacterial infection.

Antibacterials should be stopped in patients with one or more of the following -

- a positive COVID-19 laboratory or point of care result
- symptoms and blood tests (particularly lymphopenia) consistent with COVID-19 infection
- chest imaging (plain X-ray or CT scan) consistent with COVID-19 infection
- negative microbiology cultures if performed

You should seek Specialist Infection (Medical Microbiology) advice if

- patient signs and symptoms are not improving as expected
- there is a suspicion of infection with a multidrug resistant bacteria or fungus

B) Remdesivir

Remdesivir is an adenosine nucleoside triphosphate analogue, the active metabolite of which interferes with the action of SARS-CoV-2 RNA dependent RNA polymerase. Its use is managed by Department of Health and Social Care in England who have provided initiation criteria for patients who are regarded as suitable for remdesivir.

Remdesivir provides clinical benefit in COVID-19 by improving the time to recovery and may have a small effect in reducing mortality.

Remdesivir is available only in an IV infusion formulation. When used for the treatment of patients hospitalised due to symptoms of COVID-19 and requiring supplemental oxygen, it is given as a

200mg loading dose followed by 100mg daily for 4 days (5 day course in total). This may be extended to 10 days in immunocompromised patients.

Further information on eligibility criteria, dosing and monitoring can be found in the Interim Clinical Commissioning Policy and associated Clinical Guide:
https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103197
All patients require completion of an electronic BlueTeq form by a consultant prior to use to ensure they meet the initiation criteria. The system is located at: https://www.blueteq-secure.co.uk/Trust and requires prior registration.

Combination therapy

For information on interactions with concurrent medications, including those for COVID-19, please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker)

Patients may also be recruited into the RECOVERY Trial.

Pregnancy

See the latest Royal College of Obstetricians and Gynaecologists (RCOG) COVID infection in Pregnancy https://www.rcog.org.uk/guidance/coronavirus-covid-19-pregnancy-and-women-s-health/coronavirus-covid-19-infection-in-pregnancy/ All cases to be discussed with obstetric team.

References

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2.2.5.2 Patients with symptomatic hospital onset COVID-19

These patients should not routinely receive antibacterials. If the patient requires antibacterial therapy, please discuss with an Infection Specialist (Medical Microbiology).

Recent evidence suggests that antivirals and neutralising monoclonal antibodies (nMABs) significantly improve clinical outcomes in patients with COVID-19 who are at high risk of progression to severe disease and/or death. These therapies are recommended as a treatment

option for patients with symptomatic hospital onset COVID-19 showing no signs of recovery and without a new oxygen requirement.
All patients require completion of an electronic BlueTeq form prior to use to ensure they meet the initiation criteria. The system is located at: https://www.blueteq-secure.co.uk/Trust and requires prior registration.

- **First-line: Paxlovid (PF-07321332/ritonavir). 5 day course in total**

Paxlovid is a dual oral antiviral therapy containing PF-07321332 (also known as nirmatrelvir) plus ritonavir. PF-07321332 inhibits COVID-19 viral replication. Ritonavir is not active against COVID-19, but instead inhibits the CYP3A-mediated metabolism of PF-07321332 in the liver, thereby increasing plasma concentrations of PF-073213321.
The inhibitory effects of the ritonavir component of Paxlovid on hepatic CYP3A metabolic pathways means that Paxlovid will interact with other medications reliant on this pathway for clearance from the body. Some of these interactions are of significant clinical consequence, **therefore it is of utmost importance that the interaction potential between Paxlovid and each current medication is evaluated before prescribing Paxlovid.**
A number of specialist resources are available to assist with the evaluation of interactions:

1. MHRA Antiviral and nMab Clinical Guide Hospital: www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAttachment.aspx?Attachment_id=103909
2. Liverpool COVID-19 Interactions checker: www.covid19-druginteractions.org/
3. Specialist Pharmacy Service: Medicines interactions with nirmatrelvir and ritonavir (Paxlovid): www.sps.nhs.uk/wp-content/uploads/2022/01/Paxlovid-SPS-20220202.pdf
4. Paxlovid® Summary of Product Characteristics: www.medicines.org.uk/emc/product/13145

- **Second-line: remdesivir (antiviral). 3 day course in total**

- **Third-line: sotrovimab (neutralising monoclonal antibody/nMAB). Stat dose**

nMABs are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing entry of the virus into the host cell and its replication. This effectively 'neutralises' the virus particle.

Combination treatment with an nMAB and an antiviral is NOT routinely recommended

Further information on selecting the most appropriate treatment, dosing and monitoring can be found in the Interim Clinical Commissioning Policy and associated Clinical Guide: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103203

Patients who require hospital-level care for the management of acute COVID-19 illness, or those with a new supplemental oxygen requirement specifically for the management of COVID-19 symptoms may be eligible for treatment with dexamethasone, remdesivir, baricitinib or an IL6 inhibiting monoclonal antibody provided they meet the appropriate commissioning criteria. See Section 2.2.5 ("COVID-19")

2.2.6 Pleural Infection

Community Acquired**:** Amoxicillin 1g TDS IV plus metronidazole 500mg TDS IV
If penicillin allergic: co-trimoxazole 960mg BD IV plus metronidazole 500mg TDS IV.

Oral therapy: Co-amoxiclav 625mg TDS PO or if penicillin allergic co-trimoxazole 960mg BD plus metronidazole 400mg TDS.

Hospital Acquired**:** Piperacillin/tazobactam 4.5g QDS IV. Add vancomycin (see section 6.3 for dosing) if MRSA screen positive or MRSA infection in last 3 months.

If penicillin allergy, discuss with an Infection Specialist (Medical Microbiology).

Duration of therapy should be determined by a respiratory physician or an Infection Specialist (Medical Microbiology).

2.2.7 Acute Exacerbations of Bronchiectasis

Patients with an acute exacerbation of bronchiectasis should have their antibiotic therapy guided by sputum culture. Sputum should be sent before treatment is started and previous sputum cultures reviewed as a guide to therapy - BTS Guidelines, Thorax 2010, 65il-58, gives more details on the overall management of such patients.

Empirical therapy (no sputum for this episode)	**Drug and Dose**
No previous antibiotics	Amoxicillin 1g IV TDS
Previous antibiotics and not colonised by P.aeruginosa or other multi-drug resistant pathogens	Co-trimoxazole 960mg IV BD
Known colonisation with P.aeruginosa	Ceftazidime 2g IV TDS

Once a pathogen is isolated or pathogen is known at start of therapy:-

Pathogen	**Drug and Dose**
S.pneumoniae	amoxicillin 1g IV TDS
H.influenzae amoxicillin sensitive amoxicillin resistant	 Amoxicillin 1g IV TDS Co-trimoxazole 960mg IV BD
Moraxella catarrhalis	Co-trimoxazole 960mg IV BD
MRSA	Vancomycin IV. See section 6.3 for dosing.
E.coli, Klebsiella, Proteus, Citrobacter, Enterobacter etc	Ceftazidime 2g IV TDS
P.aeruginosa	Ceftazidime 2g IV TDS

All patients should be treated for 14 days. Many patients may be suitable for outpatient hospital at home iv therapy including infusion via elastomeric pumps; such patients should be discussed with an Infection Specialist (Medical Microbiology) and Hospital at Home staff. Consider oral switch when appropriate.

Patients who are infected with P.aeruginosa may also benefit from inhalational therapy, the dosing being:

Drug	**Dose**	**Frequency**
Gentamicin	80mg	BD
Tobramycin nebs	300mg	BD
Colistin	1-2 MU (million units)	BD

2.3 Central Nervous System

Community acquired bacterial meningitis

Empirical therapy: ceftriaxone 2g BD IV 10 days

If patient is ≥60 years old, pregnant or immunocompromised consider the addition of amoxicillin 2g 4hrly IV to cover Listeriosis. If patient is penicillin allergic add co-trimoxazole 120mg/kg IV daily in four divided doses instead.

Penicillin allergy – discuss with a Medical Microbiologist

Once the aetiology is known:

Neisseria meningitidis	amoxicillin 2g 4hrly IV 5 days
Streptococcus pneumonia - penicillin susceptible	amoxicillin 2g 4hrly 10 days
Streptococcus pneumoniae – penicillin non susceptible	discuss with medical microbiologist
No pathogen isolated	ceftriaxone 2g BD IV 10 days
Other pathogens	Discuss with a Medical Microbiologist

Consider adjunctive treatment with dexamethasone 10mg QDS IV for 4 days, especially if pneumococcal meningitis in adults, starting before or within 12 hours of the first dose of antibacterial. Avoid dexamethasone in septic shock or if immunocompromised or in post operative meningitis.

For neurosurgical infection, see section 5.1.

Herpes Simplex Encephalitis

Aciclovir 10mg/kg IV TDS for 14-21 days

Treatment should be reviewed once the results of the CSF viral PCR are available. Discuss with a Medical Microbiologist.

2.4 Urinary Tract

Diagnosis

Urinary tract infections (UTIs) typically present as pyuria, dysuria and suprapubic tenderness. Pyelonephritis is a syndrome associated with local symptoms as well as flank or back pain. Complicated UTIs are those in patients with a predisposition to persistent infection or treatment failure such as urinary stricture, tumour, stones, obstruction, stents, a catheter or pregnancy; or where systemic signs are present.

Signs and symptoms compatible with catheter-associated UTI include: new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; costovertebral angle tenderness; acute haematuria; pelvic discomfort dysuria, urgent or frequent urination, or supra-pubic pain or tenderness in patients whose catheters have been removed.

Management

- **Ensure urine cultures are taken prior to starting antibiotics**.
- Check and monitor temperature, respiratory rate, pulse, blood pressure and mental status.
- If the patient has a NEWS of 5 (or 3 in one parameter) complete a Sepsis Screening Tool, take blood cultures and start antibiotics within 1 hour.
- Check and monitor U&Es, CRP, LFTs and FBC.
- Patients should be assessed for volume depletion and may require intravenous fluids.
- Review the patient's previous cultures and start treatment according to table below.
- **Do not prescribe antibiotics based on urinary dipstick alone**.

Treatment

Classification	**Management**	**Antibiotic therapy**
Review at 24-48hrs with culture results and susceptibility tests and aim to switch to an oral agent. IV antibiotics can be de-escalated once IV/oral switch criteria are met. Stop antibiotics if infection has been ruled out. **Record all decisions in the notes**. **State duration and indication on the drug chart.**		
Community acquired infections are those presenting on, or within, 48 hours of admission in patients who have not been hospitalised in the previous 3 months.		
Uncomplicated UTI	If possible delay starting therapy until urine cultures are reported	First line: Nitrofurantoin 50mg QDS PO Duration: women 3 days, men 5 days Second line: Pivmecillinam 400 mg TDS PO Duration: women 3 days, men 5 days Please note that pivmecillinam is a penicillin. In patients with penicillin allergy discuss with a microbiologist.
Complicated UTI	If the patient has a catheter, consider removal if possible or replacement once antimicrobial therapy has been started	Patients requiring IV therapy: gentamicin IV (see section 6.1 for dosing). Duration: 5 days. If the patient's eGFR is <20ml/min: ciprofloxacin 500mg PO BD for 2 doses* and then OD. Duration: 5 days. Check previous urine samples for antibiotic resistance. Note oral ciprofloxacin is well absorbed – IV therapy is only required if patient is nil by mouth. Provide MHRA patient information leaflet about quinolone side effects *off-label dose Patients requiring oral therapy: nitrofurantoin 50mg QDS or pivmecillinam 400mg TDS for 5 days ***If eGFR <30ml/min do not use Nitrofurantoin. If eGFR 30-45mls/min use with caution and only if there is no alternative.***
Acute pyelonephritis In female patients	Consider taking blood cultures. For pregnant	Gentamicin IV single dose (see section 6.1 for dosing) plus ciprofloxacin 500mg BD PO for 7 days. If the patient's eGFR is <20ml/min, discuss with a

≤50 years and who are fit for discharge (i.e. patients in ED/AMU)	patients refer to O&G guidelines.	medical microbiologist Provide MHRA patient information leaflet about quinolone side effects Do not use nitrofurantoin or pivmecillinam due to poor tissue concentrations.
All other patients with acute pyelonephritis	Take blood cultures	Gentamicin IV (see section 6.1 for dosing). Total duration: 7 days. Discuss oral step down with a Microbiologist. If the patient's eGFR is <20ml/min, discuss with a medical microbiologist. Do not use nitrofurantoin or pivmecillinam due to poor tissue concentrations.
Catheter associated UTI		Treat as for complicated UTI Do not offer antibiotic prophylaxis routinely when changing catheters in patients with long term indwelling urinary catheters. Consider antibiotic prophylaxis in those with a history of symptomatic UTI after catheter change or who experience trauma during catheterisation. If indicated, a single dose of gentamicin 80mg IM/IV can be given but consider prior urine culture and sensitivity results
Epididymo-orchitis	Assess risk for sexually transmitted infection (STI): -age >35 low risk for STI -low-risk sexual history -previous urological instrumentation/ catheterisation and/ or known urinary tract abnormality – low risk for STI	Low risk for STI: ciprofloxacin 500 mg BD PO for 10 days. Provide MHRA patient information leaflet about quinolone side effects High risk for STI: doxycycline 100 mg BD for 10-14 days PO plus single dose ceftriaxone 1g IM/IV Consider referring patient and partner to GUM clinic.
Prostatitis		Ciprofloxacin 500mg BD PO for 28 days. Provide MHRA patient information leaflet about quinolone side effects
Hospital acquired infections are those presenting 48 hours after admission and in patients who have been hospitalised in the previous 3 months.		
UTI		Patients requiring IV therapy: Amikacin IV (see section 6.2 for dosing) Total duration: 5 days If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist. Patients requiring oral therapy: Nitrofurantoin 50mg QDS PO for 5 days Second line: Pivmecillinam 400 mg TDS PO for 5 days
Vaginal candidiasis		Clotrimazole 200mg OD PV for 3 days

Notes: ***If eGFR <30ml/min do not use Nitrofurantoin. If eGFR 30-45mls/min use with caution and only if there is no alternative.***

References

PHE. Management of infection guidance for primary care for consultation and local adaptation https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

SIGN. Management of suspected bacterial urinary tract infection in adults http://www.sign.ac.uk/media/1051/sign88.pdf

[1] BASHH. 2010 United Kingdom national guideline for the management of epididymo-orchitis http://www.bashh.org/documents/3546.pdf

2.5 Blood

ANTIBIOTICS MUST BE GIVEN WITHIN ONE HOUR OF DIAGNOSIS FOR SEVERE SEPSIS

Antibiotic management of severe sepsis and septic shock requiring intensive care

Patients with sepsis and septic shock will require intensive care. For patients with hypotension, tachycardia, temperatures >38°C or <36°C, tachypnea, poor renal function and other variables associated with severe sepsis, early appropriate antimicrobial therapy has a major impact on outcome. The Surviving Sepsis Campaign recommends the following in terms of antibiotic therapy.

- begin IV antibiotics as early as possible, and always within one hour of recognising severe sepsis and septic shock
- broad spectrum: one or more agents active against the likely pathogens
- reassess the regimen daily to optimise efficacy, prevent resistance, avoid toxicity and minimise costs
- combination therapy for no more than 3-5 days and de-escalate following susceptibilities
- duration of therapy is typically 7-10 days
- stop antibiotics if cause found to be non-infectious

Patients without severe sepsis or septic shock often also require intensive care. In all patients transferring to ICU, aminoglycosides should be avoided and substitutes given. Discussion with an intensivist and medical microbiologist is essential.

2.5.1 Community acquired sepsis (focus unknown)

Amoxicillin 1g TDS IV + flucloxacillin 2g QDS IV + gentamicin IV (see section 6.1 for dosing).

penicillin allergy: Establish nature of allergy and discuss with a Medical Microbiologist.

If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist.

Add metronidazole 500mg TDS IV if anaerobic infection suspected. If MRSA infection suspected (previous MRSA infection, colonised with MRSA), discuss with medical microbiologist.

2.5.2 Community acquired sepsis (origin pneumonia and/or urinary tract infection)

Amoxicillin 1g TDS IV + azithromycin 500mg OD IV + gentamicin IV (see section 6.1 for dosing)

penicillin allergy: Establish nature of allergy and discuss with a Medical Microbiologist.

If the patient's eGFR is <20ml/min, please discuss with a medical microbiologist.

2.5.3 Hospital acquired sepsis (focus unknown)

discuss with medical microbiologist

Please note: do not treat with combination of vancomycin plus gentamicin, as the risk of nephrotoxicity is significant.

2.6 Antibiotic Management of Patients with Neutropenic Sepsis

This summary is based on NBT Policy CP17 (Feb 2016) "Management of Patients at Risk of Neutropenic Sepsis Policy". It should be read in conjunction with the whole policy which can be accessed here.

The policy is limited to those who are neutropenic secondary to haemato-oncology diagnosis or treatment.

- Neutropenia is defined as a neutrophil count of $<0.5 \times 10^9$/L.
- Fever is defined as an oral or tympanic membrane temperature of ≥38°C sustained for 1 hour or a single temperature of ≥38.5°C.
- Neutropenic sepsis, also called neutropenic fever, is diagnosed in those having anti-cancer treatment with a neutrophil count of $<0.5 \times 10^9$/L and a temperature of ≥38°C **or** other signs and symptoms consistent with infection.

If neutropenic fever is not confirmed - i.e. the neutrophil count is $>1.0 \times 10^9$ stop piperacillin/tazobactam and follow the NBT Antibiotic Guidelines.

The MASCC Index is used to categorise oncology and haematology patients into severe and non-severe groups. If the MASCC Index score is ≥21, treat as non-severe (low risk), if the score is <21, treat as severe (high risk).

Patients at low risk of septic complications

Consider outpatient antibiotic therapy for patients with confirmed neutropenic sepsis and a low risk of developing septic complications, taking into account the patient's social and clinical circumstances and discussing with them the need to return to hospital promptly if a problem develops.

MASCC Scoring chart

CHARACTERISTICS		SCORE
Age	≥ 60 years	0
	< 60 years	2
Patient dehydrated, requiring fluids	Yes	0
	No	3
Patient hypotensive	Systolic BP <90	0
	Systolic BP ≥90	5
Does the patient have COPD? (Chronic Obstructive Pulmonary Disease)	Yes	0
	No	4
Does the patient have a solid tumour or no previous fungal infection in a haematological malignancy?	Solid Tumour or no previous infection in haematological malignancy	4
	Haematological malignancy with previous fungal infection	0
Does the patient have symptoms related to this febrile neutropenic episode?	None or mild symptoms	5
	Moderate symptoms	3
	Severe symptoms	0
Was the patient already an inpatient before this episode of febrile neutropenia?	Already an inpatient	0
	Admitted with this episode	3

Treatment of non-severe patients - Modify antibiotic choice according to previous microbiology and risk assessment for CPE

CATEGORY		ANTIBIOTIC	COURSE LENGTH	COMMENTS
Non-severe MASCC Index Score ≥21	**First Line** Patients who have had ciprofloxacin prophylaxis or treatment in the last 6 weeks should be treated as severe	**Co-amoxiclav** 625mg PO TDS PLUS **Ciprofloxacin** 750mg PO BD Provide MHRA patient information leaflet about quinolone side effects	7 days 7 days	Consider outpatient therapy IF: • Patient is mentally competent • Lives near the hospital (within one hour) • Has a thermometer at home • Has someone at home all of the time • Has access to transport and a telephone
	Penicillin (or beta lactam allergic)	**Clindamycin** 300mg QDS PO PLUS **Ciprofloxacin** 750mg PO BD Provide MHRA patient information leaflet about quinolone side effects	7 days	
	Second line	Switch to severe IV treatment	7 days	

Treatment of severe patients - Modify antibiotic choice according to previous microbiology and risk assessment for CPE

CATEGORY		ANTIBIOTIC	COURSE LENGTH	COMMENTS
Severe MASCC Index Score <21	**First Line**	**IV piperacillin/tazobactam** 4.5g QDS If penicillin allergic establish nature and discuss with medical microbiologist	7 days	Do not switch empirical antibiotics in patients with unresponsive fever unless there is clinical deterioration or a microbiological indication. If no improvement after 48-72 hours discuss with Haematology or Microbiology If no improvement 4-
	If evidence of line/IV access or hypotensive then add:	**IV vancomycin** **Please refer to Trust Guidelines on dosing**		

	If fever persists at 48 hours and central line add: **Consider stopping antibiotics if:**	**IV vancomycin** Neutrophils >0.5x10^9/L, patient is well and apyrexial for 3 days Neutrophils <0.5x10^9/L, patient is well and apyrexial for 5 days		5 days from start of antibiotics discuss antifungal investigations/therapy with Haematology or Microbiology. Consider switching to oral therapy after 48 hours if patient low risk.

2.7 Skin

Oral therapy is suitable for many patients with cellulitis. IV therapy should be reserved for the following: severe and rapidly spreading infection, systemic signs of sepsis, immuno compromised patients such as diabetics and those unable to tolerate oral medication. However, if initial treatment is delayed, cellulitis may result in severe tissue damage, taking weeks to recover. This recovery period is not shortened by extended duration of antibiotic.

Review antibiotics at 48-72 hours. Therapy should be changed to a narrow spectrum agent once a definite pathogen has been identified.
IV antibiotics should be de-escalated once IV/oral switch criteria are met. Stop antibiotics if infection has been ruled out. Record all decisions in the notes. State the duration and indication on the drug chart.

Cellulitis/ erysipelas	flucloxacillin 500mg QDS PO or 2g QDS IV for 5 days and then review. Complicated infections may require up to 14 days. For outpatient IV therapy of cellulitis: ceftriaxone 1-2g OD or teicoplanin (see section 6.4 for dosing)	In penicillin allergy use clindamycin 300mg QDS PO or 600mg QDS IV
Animal and human bites	Co-amoxiclav 1.2g TDS IV or co-amoxiclav 625mg TDS PO for 5 days	For patients with penicillin allergy clindamycin 300mg PO QDS (450mg IV) with or without ciprofloxacin* 750mg BD PO can be used for 5 days, but discuss with a Medical Microbiologist. * Provide MHRA patient information leaflet about quinolone side effects
Wound infection following clean surgery	Flucloxacillin 500mg QDS PO or 2g QDS IV for 5 days	Penicillin allergy: clindamycin 300mg QDS PO or 450mg QDS IV for 5 days
Wound infection following contaminated surgery	Co-trimoxazole 960mg IV BD + metronidazole 500mg IV TDS for 5 days Oral step down: co-trimoxazole 960mg BD PO + metronidazole 400mg TDS PO	
Perianal infection/abscess	Co-trimoxazole 960mg IV BD + metronidazole 500mg IV TDS for 5 days Oral step down: co-trimoxazole 960mg BD PO + metronidazole 400mg TDS PO	

Cellulitis at a cannula site	Flucloxacillin 500mg QDS PO or 2g QDS IV for 5 days	Penicillin allergy: clindamycin 300mg QDS PO or 450mg QDS IV for 5 days
Cellulitis in a current injecting drug user	Flucloxacillin 500mg QDS PO or 2g QDS IV for 5 days. If known to be colonised with MRSA give vancomycin (see section 6.3 for dosing)	Penicillin allergy: clindamycin 300mg QDS PO or 450mg QDS IV for 5 days
Mastitis and breast abscesses	Flucloxacillin 500mg QDS PO or 2g QDS IV for 5 days	Penicillin allergy: clindamycin 300mg QDS PO or 450mg QDS IV for 5 days

Necrotising fasciitis	Piperacillin-tazobactam 4.5g IV QDS plus clindamycin 600mg IV QDS If the patient is colonised with MRSA, has risk factors for MRSA, or is an IVDU – add vancomycin (see section 6.2 for dosing)	penicillin allergy – consult a Medical Microbiologist

If MRSA is suspected or proven to be the cause of infection, see MRSA treatment policy or discuss with a Medical Microbiologist

2.8 Diabetes mellitus foot infection

Antibiotic therapy is only one part of the management of diabetic foot infection. The Diabetic and Vascular team should be consulted on individual patient management. Please also refer to the Diabetes Foot Team In-patient Referral Pathway.

PEDIS grade	Definition	Treatment	Penicillin Allergic	Length of Treatment
4	**Septic** (Fever Tachycardia Hypotension Tachypnoea)	Piperacillin/tazobactam 4.5g TDS IV Discuss with a Medical Microbiologist for oral step down options	Clindamycin 450-600mg QDS IV + gentamicin IV (see section 6.1 for dosing)	Usually 14 days initially
3	**Deeper infection** **or** lymphangitis **or** >2cm erythema **or** failure of previous treatment	***Preferred route for inpatients*** **Flucloxacillin** 2g QDS **IV** Add **Metronidazole** 500mg TDS IV if anaerobic component suspected	**Clindamycin** 450-600mg QDS IV + **Ciprofloxacin** 500mg BD PO Provide MHRA patient information leaflet about quinolone side effects	Usually 14 days initially
2	Skin/sub-cutaneous infection only **and** <2cm erythema **and <u>no previous</u>** antibiotic treatment (in last 3 months)	***Preferred route for outpatients*** **Flucloxacillin** 500mg-1g QDS PO if suspected anaerobic component add metronidazole 400mg TDS PO or **Co-amoxiclav** 625mg TDS PO	**Clindamycin** 300 mg QDS PO	7 days
1	Not infected	NIL	NIL	

- If high risk for MRSA (previous MRSA colonisation/infection, hospital admission within 6 months, nursing home resident) see MRSA treatment guide.

- Osteomyelitis secondary to diabetic foot complications may be due to a wide variety of organisms. The specimens of choice are bone biopsy and deep curettage. Swabs are of limited value. Suggest discuss with medical microbiologist/diabetic foot team regards empirical and definitive therapy.

2.9 Treatment of infection in Hepatology

2.9.1 Treatment of spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis

Piperacillin/tazobactam 4.5g IV TDS for 5 days

Empirical therapy should be started in patients with an ascitic fluid neutrophil count of >250 cells/ml. Patients who fail to respond or where secondary peritonitis is suspected should be discussed with a Medical Microbiologist. Patients recovering from an episode of SBP should receive continuous prophylaxis.

2.9.2 Prophylaxis of spontaneous bacterial peritonitis (SBP)

Co-trimoxazole 960mg PO OD long term

2.9.3 Prevention of infection in upper GI haemorrhage in patients with liver cirrhosis

Piperacillin/tazobactam 4.5g IV TDS for 5 days

Bacterial infections occur in about 20% of patients with liver cirrhosis with upper gastrointestinal bleeding within 48 hours of admission and the incidence increases to 35–66% within two weeks. Patients with liver cirrhosis and upper GI bleeding should receive empirical prophylaxis.

2.10 Eye

Purulent conjunctivitis: Chloramphenicol 0.5% eye drops every 2 hours for 2 days and then 4 hourly for 48 hours after resolution of symptoms

2.11 Ear, nose and throat

Sore throat: phenoxymethylpenicillin 500mg QDS PO for 5 days

Sinusitis: phenoxymethylpenicillin 500mg QDS PO for 5 days

Otitis externa: acetic acid spray. One spray TDS for 7 days

Otitis media: No antibiotics unless systemically unwell, complications or symptoms for > 4 days. amoxicillin 500mg TDS PO or clarithromycin 500mg BD PO for 5 days

3 ANTIBACTERIAL PROPHYLAXIS

3.1 Non-Surgical Prophylaxis – see BNF for full details.
For vaccinations pre or post splenectomy see appendix A

3.2 Surgical Prophylaxis

3.2.1 Best practice for prescribing an antimicrobial for peri-operative prophylaxis

Best practice point	Action
Need for prophylaxis and guideline choice of agents	Prescribe prophylaxis with appropriate agents according to NBT guidelines. Use appropriate alternatives for patients with beta-lactam allergy
Timing	Administer antibiotics within 60-minutes prior to incision (or tourniquet)
Repeat doses	Single dose is indicated for majority of procedures. The reason for antibiotic administration beyond one dose should be documented and comply with criteria below: • Significant intra-operative blood loss - >1.5 litre (re-dose following fluid replacement). • Prolonged procedures (>6hours) • Primary arthroplasty, where 24 hours prophylaxis is acceptable.
Ensure allergies are clearly documented	All allergies must be recorded on the front of the drug chart and anaesthetic record. The nature of the allergy/reaction should also be stated.
MRSA positive patients	Decolonisation therapy is recommended prior to surgery and antibiotic prophylaxis should include cover for MRSA.

3.2.2 Principles of Prophylaxis

Type of surgery	Definition	Prophylaxis
Clean	Operations in which no inflammation encountered and the respiratory, alimentary or genitourinary tracts are not entered. There is no break in aseptic operating technique.	No prophylaxis (except in implantation)
Clean-Contaminated	Operations in which the respiratory, alimentary or genito-urinary tract are entered but without significant spillage.	Single dose **except for primary arthroplasty/ implant surgery**
Contaminated	Operations where acute inflammation (without pus) is encountered, or where there is visible contamination of the wound. Examples include gross spillage from a hollow viscus during the operation or compound/open injuries operated on within 4 hours.	5 day treatment course in addition to prophylaxis
Dirty	Operations in the presence of pus, where there is a previously perforated hollow viscus, or compound/open injuries more than 4 hours old.	5 day treatment course in addition to prophylaxis

3.2.3 Timing of Prophylaxis

The aim of prophylaxis is to have maximum tissue levels at the time of first incision (the only exception is where microbiological specimens are to be taken, in which case prophylaxis should be given immediately after specimens have been obtained). Oral and intramuscular prophylaxis is usually administered 1 hour pre-op, whereas IV antibiotics are

given on starting anaesthesia. However give prophylaxis earlier for operations in which a tourniquet is used.

3.2.4 Pre-operative risk assessment for likelihood of MRSA carriage for patients who have not been screened prior to surgery.

The following questions will enable a quick risk assessment of MRSA status of those patients who have declined screening for MRSA or have not been screened for another reason prior to surgery. These are based on current recognised risk factors for MRSA carriage.

1. **Is the patient known to be MRSA positive on a previous occasion?** If so, this should be clearly noted by nursing staff, the patient may be put at the end of the list for infection control reasons.

2. **Has the patient come from a nursing home or directly from another healthcare establishment (hospital transfer), or directly from abroad?** See patients addressograph label, pre-op note may state transfer to NBT for surgery.

3. **Does the patient have a long term urinary catheter?** The absence of a fluid balance chart means the patient is more likely to have a long-term catheter than one recently inserted in hospital.

4. **Is the patient known to be a frequent or recent hospital attender?** As suggested by multiple significant co-morbidities on the anaesthetic notes, recent anaesthetics, very thick case notes or X ray folders etc.

If <u>YES to any</u> of the above, then MRSA colonisation is more likely and it would be reasonable to prophylax as for a known MRSA positive patient.

If <u>NO to all</u> above questions, use routine prophylaxis.
Where information is not available please make a judgement on whether it is likely that the patient will have had an opportunity to acquire MRSA. For example:

- A young adult with acute appendicitis, unlikely to be a regular hospital attender and is very unlikely to have MRSA
- An elderly patient with several drug allergies, or multiple X rays or very thick notes, is likely to have had several healthcare interventions in the past - may well have acquired MRSA.

Why not just prophylax every patient as if potentially MRSA colonised?

- Vancomycin and teicoplanin are not as effective antibiotics as the penicillin-based alternatives (e.g. flucloxacillin) for MSSA infection.
- They take longer to prepare and administer
- They are much more expensive
- We must avoid selecting for resistance to these antibiotics.
- <1% elective patients when screened are colonised with MRSA

<u>Note</u> These guidelines will not accurately identify all potentially colonised cases and do not substitute for clear documentation of MRSA screening results by the patient's clinical team.

For patients known to be MRSA positive or who have risk factors replace amoxicillin or flucloxacillin with teicoplanin 400mg IV (600mg if patient is >100kg) or add teicoplanin 400mg IV (600mg if patient is >100kg) to existing regime if no amoxicillin/flucloxacillin to replace.

3.2.5 Prophylaxis for patients with other multidrug resistant pathogens

Patients known to be colonised pre operatively with pathogens likely to be resistant prophylaxis should have their antibiotic prophylaxis discussed with a medical microbiologist pre-operatively.

3.2.6 Duration of operative procedures

For prolonged procedures (>6hours) and/or major blood loss, additional intra operative doses of 50% of the initial dose should be administered at 4h intervals (8 hourly for gentamicin) for the duration of the procedure.

3.2.7 Patients with a penicillin allergy

Investigate the nature of the penicillin allergy (see section 7). For patients who are allergic to penicillin replace the penicillin with teicoplanin 400mg IV (600mg if patient is >100kg). For patients with renal impairment see section 6.1 for gentamicin dose reduction

3.2.8 In patients with impaired renal function a reduced doe of gentamicin should be given as per the table below.

creatine clearance (eGFR)	Dose	
	Higher dose (where 24 hour coverage is needed)	**Standard dose**
>80ml/min	5mg/kg	3mg/kg
40-80ml/min	3.5mg/kg	2mg/kg
<40ml/min	2mg/kg	1mg/kg

- 5mg/kg dose is used for prophylaxis in orthopaedic surgery, except lower limb amputation
- obese patient BMI ≥30kg/m^2, use ideal body weight to calculate dose

All regimens in the table below are single doses unless stated otherwise.

3.2.9 Upper gastrointestinal		**Penicillin allergy**	**comments**
Oesophageal surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV+ gentamicin 3mg/kg IV	
Stomach and duodenal	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Gastric bypass surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Small intestine surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Open/laparoscopic bariatric surgery (e.g. gastric band)	amoxicillin 1g iv + gentamicin 3mg/kg iv	teicoplanin 600mg IV+ gentamicin 3mg/kg IV	

3.2.10 Lower gastrointestinal		Penicillin allergy	comments
Appendectomy	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mgIV	
Colorectal surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Emergency laparotomy	Co-trimoxazole 960mg IV + metronidazole 500mg IV	Co-trimoxazole 960mg IV + metronidazole 500mg IV	
3.2.11 Abdomen		**Penicillin allergy**	**comments**
Hernia repair-groin without mesh	Prophylaxis not usually recommended		
Hernia repair with mesh	flucloxacillin 1g IV + gentamicin 3mg/kg +/- metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV+/- metronidazole 500mg IV	
Diagnostic endoscopic procedures	Prophylaxis not recommended		
PEG insertion	Flucloxacillin 1g IV + gentamicin 3mg/kg IV		
ERCP	Gentamicin 3mg/kg IV or ciprofloxacin 750mg PO single dose		ciprofloxacin should be given 2 hours before the procedure
Splenectomy	Prophylaxis not recommended		See Appendix A for post-surgical prophylaxis and vaccination
3.2.12 Hepatobiliary		**Penicillin allergy**	**comments**
Bile duct surgery	Gentamicin 3mg/kg IV		
Pancreatic surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Liver surgery	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Liver biopsy	Prophylaxis not recommended		
Gall bladder surgery (open)	Flucloxacillin 1g IV + gentamicin 3mg/kg	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Gall bladder surgery (laparoscopic)	Prophylaxis not recommended.		

Gall bladder surgery (laparoscopic) in high risk patients	gentamicin 3mg/kg IV	gentamicin 3mg/kg IV	High risk: intraoperative cholangiogram, bile spillage, conversion to laparotomy, acute cholecystitis/pancreatitis , jaundice, pregnancy, immunosuppression, insertion of prosthetic devices.
3.2.13 Uro-genital		**Penicillin allergy**	**comments**
Transrectal prostate biopsy	ciprofloxacin 750mg PO 2 hours before the procedure. If resistance/contraindication to ciprofloxacin give gentamicin 3mg/kg IV		
Shock wave lithotripsy	Pre-procedural antibiotics do not significantly reduce the risk of UTI and fever in patients undergoing ESWL, but should be considered in patients at high risk of infectious complications (i.e. patients with large stone burden, associated pyuria, history of pyelonephritis, and adjunctive operative procedure including stent, nephrostomy insertion, PCNL or ureteroscopy). For high risk patients give gentamicin 3mg/kg IV stat		
Routine cystoscopy	Prophylaxis not recommended		Check urine cultures especially if known/recurrent UTI. See BUI pathway here (link)
Traumatic cystoscopy/ ureteroscopy	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Percutaneous nephrolithotomy	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Endoscopic ureteric stone fragmentation/ removal	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Transurethral resection of prostate	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Transurethral resection of bladder tumours	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	Prophylaxis not usually recommended but consider in high risk patients and large tumours.
Radical cystectomy	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Open prostatectomy	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Formation of ileal conduit or neo-bladder	Amoxicillin 1g IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
Circumcision	Prophylaxis not recommended.		
Insertion of an	Flucloxacillin 1g IV +	Teicoplanin 400mg IV	

artificial urinary sphincter	gentamicin 3mg/kg IV + metronidazole 500mg IV	+ gentamicin 3mg/kg IV + metronidazole 500mg IV	
Insertion of urethroplasty	Amoxicillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
3.2.14 Gynaecological		**Penicillin allergy**	**comments**
Abdominal hysterectomy	Co-amoxiclav 1.2g IV	**Non-type 1 penicillin allergy:** cefuroxime 1.5g IV + metronidazole 500mg IV	
Vaginal hysterectomy	Co-amoxiclav 1.2g IV	**Non-type 1 penicillin allergy:** cefuroxime 1.5g IV + metronidazole 500mg IV	
Caesarean section	Cefuroxime 1.5g IV + metronidazole 1g PR		Give clindamycin 600mg IV if type 1 allergy. Give pre-skin incision
Assisted delivery	Co-amoxiclav 1.2g IV	Clindamycin 300mg IV	To be given as soon as possible after birth and definitely within 6 hours of birth
Third or fourth degree perineal tears	Cefuroxime 1.5g IV + metronidazole 500mg IV		Give clindamycin 600mg IV if type 1 allergy
Manual removal of the placenta	Cefuroxime 1.5g IV + metronidazole 500mg IV		Give clindamycin 600mg IV if type 1 allergy. Prophylaxis should be considered
Induced abortion	Co-amoxiclav 1.2g IV	**Non-type 1 penicillin allergy:** cefuroxime 1.5g IV + metronidazole 1g PR	Give clindamycin 600mg IV if type 1 allergy
Evacuation of incomplete miscarriage	Prophylaxis not recommended		
Intrauterine contraceptive device insertion	Prophylaxis not recommended		
3.2.15 Orthopaedic surgery		**Penicillin allergy or MRSA risk**	**comments**
Arthroscopy	Prophylaxis not recommended		
Arthroplasty	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 5mg/kg IV	
Open fracture – prophylaxis at time of surgical intervention	Ceftriaxone 2g IV stat	Teicoplanin 400mg IV stat + gentamicin 5mg/kg IV stat	Stat dose(s) only - given at time of surgical intervention
Open surgery for closed fracture	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 5mg/kg IV	

Hip fracture	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 5mg/kg IV	
Orthopaedic surgery (without implant)	Prophylaxis not recommended		
Lower limb amputation including trauma	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
3.2.16 Vascular surgery		**Penicillin allergy**	**comments**
Abdominal and lower limb arterial reconstruction	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	Add metronidazole 500mg IV if aortic aneurysm repair.
Lower limb amputation	See above		
Renal transplantation	See kidney transplant protocol		
Tenchkoff insertion	See guidelines for peritoneal dialysis		
3.2.17 Breast surgery		**Penicillin allergy**	**comments**
Breast cancer surgery	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Breast reshaping procedures	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Breast surgery with implant	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
3.2.18 Plastic surgery		**Penicillin allergy**	**comments**
Plastic surgery	Flucloxaxillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Prevention of infection during leech therapy	ciprofloxacin 500mg BD PO for duration of contact. Provide MHRA patient information leaflet about quinolone side effects		
Open fracture – prophylaxis at time of surgical intervention	Ceftriaxone 2g IV stat	**(Or MRSA risk)** Teicoplanin 400mg IV stat + gentamicin 5mg/kg IV stat	Stat dose(s) only - given at time of surgical intervention
3.2.19 Trauma surgery		**Penicillin allergy or MRSA risk**	**comments**
Penetrating trauma to CNS (cranio-cerebral)	Ceftriaxone 2g IV + metronidazole 500mg IV	Discuss with a medical microbiologist	If gross spillage from a viscus that may include non-purulent material, dirty traumatic wounds, faecal contamination, foreign body, de-vitalised viscus or pus encountered from any source during surgery then give a 5 day treatment course
Maxillofacial	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Thoracic	ceftriaxone 2g IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Abdominal (with peritonitis)	ceftriaxone 2g IV metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole	

		500mgIV	
Limbs	ceftriaxone 2g IV metronidazole 500mg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + metronidazole 500mg IV	
3.2.20 Cardiac implantable electronic device		**Penicillin allergy**	**comments**
Insertion of cardiac implantable electronic device	Flucloxacillin 1g IV	Teicoplanin 400mg IV	
3.2.21 Neurosurgery		**Penicillin allergy**	**comments**
Clean non implant or minor implants (titanium mini plate, Brantigan cage, odontoid screw)	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV+ gentamicin 3mg/kg IV	
Major non shunt implants (acrylic/titanium cranioplasty, major spinal implants)	Flucloxacillin 1g IV + gentamicin 3mg/kg IV	Teicoplanin 400mg IV + gentamicin 3mg/kg IV	
Clean contaminated (one or more cranial air sinuses, crossed or access via nasopharynx or oropharynx)	Co-trimoxazole 960mg IV + metronidazole 500mg IV		
Shunt implant or revision	flucloxacillin 1g IV + gentamicin 3mg/kg IV + intraventricular vancomycin 10mg + intraventricular gentamicin 3mg	Teicoplanin 400mg IV + gentamicin 3mg/kg IV + intraventricular vancomycin 10mg + intraventricular gentamicin 3mg	
Implant of an Ommaya reservoir	intraventricular vancomycin 10mg + intraventricular gentamicin 3mg		
CSF leak (rhinorrhoea or otorrhoea)	Prophylaxis not required		
Penetrating cranio-cerebral injuries (gunshot wounds, other causes)	ceftriaxone 2g IV + metronidazole 500mg IV	Discuss with a medical microbiologist	If contaminated give a 5 day treatment course

All doses are single dose unless specified.
For prolonged operative procedures (> 6 hours and/or major blood loss), additional intra-operative doses of 50% of the initial dose should be administered every 4 hours (every 8 hours for gentamicin for the duration of the procedure)

For patients known to be MRSA positive or who have other risk factors (3.2.1) replace flucloxacillin with teicoplanin 400mg IV (unless giving co-trimoxazole).

References

- BSAC/HIS/ICNA WP recommendations - JHI, 2006, 63 Suppl S3-4 – *Guidelines for MRSA in healthcare facilities: Screening*
- Local experience/root cause analysis findings re higher risk of MRSA in CSU from patients with long term catheters
- Start Smart then Focus. Advisory committee on antimicrobial resistance and healthcare associated infection (ARHAI), November 2011
- NICE clinical guideline 74. Surgical site infection, October 2008
- NICE clinical guideline 132. Caesarean section, November 2011
- SIGN antibiotic prophylaxis in surgery, July 2008, update 2014
- Peterson & Waterman 2011, Exp Rev Anti Infect Ther: 9(1) 181-96

4.1 *Clostridioides difficile* infection: treatment guidelines

See also the NBT Infection Control Policy for *Clostridioides difficile* (*Clostridium difficile*)

Background

Patients prescribed an antimicrobial will often experience transient episodes of diarrhoea. The majority of cases of loose stools following antibiotic treatment are not caused by *Clostridioides difficile*. However, *C.difficile* associated colitis can cause considerable morbidity and mortality.

Action on suspicion of a case of *C.difficile* diarrhoea

- before starting treatment, send a sample of faeces for detection of *C.difficile* toxin
- treatment should not be delayed awaiting laboratory *C.difficile* toxin results. Commence treatment if the suspicion is high or if disease severity is severe
- implement infection control measures including single room isolation. If necessary, discuss with Infection Control regarding best placement for the patient
- discontinue all other antibiotics at diagnosis unless there is a very clear clinical need. Discuss with a medical microbiologist if an alternative is required
- review the need for proton pump inhibitors (PPI) and stop unless a clear indication for PPI therapy
- avoid the use of antimotility medicines such as loperamide
- replace fluid losses and correct electrolyte imbalance
- use thorough hand washing techniques with soap and water. Gloves and apron should be worn when caring for patients infected with *C.difficile* – please refer to the Infection Control Policy on *C.difficile* for further details
- observe closely for signs of worsening condition or toxic megacolon. Patients with worsening symptoms should be referred to a Medical Microbiologist and reviewed urgently by a surgical team

Severity assessment of *C.difficile* infection

These have been defined by Public Health England (PHE 2013).

Mild: no increase in peripheral WBC, typically fewer than 3 episodes of loose stools per day.

Moderate: increase in peripheral WBC (but less than $15x10^9$/L), typically 3-5 episodes of loose stools per day.

Severe: peripheral WBC of $>15x10^9$/L, or an acutely increased serum creatinine (>50% increase over baseline) or temperature of >38.5^{o}C, or evidence of severe colitis (abdominal or radiological signs). The number of stools per day may be less reliable.

Life threatening: signs and symptoms include hypotension, partial or complete ileus, toxic megacolon or CT evidence severe disease.

Antimicrobial therapy

Situation	Antibiotic, dose, length
Antimicrobials for life threatening *C.difficile* infection	Seek advice from a medical microbiologist
First line therapy of a first episode of mild, moderate or severe *C.difficile* infection	vancomycin, 125mg PO 6hrly for 10 days
Second line therapy for a first episode if vancomycin ineffective	Seek advice from a medical microbiologist
Antibiotics for *C.difficile* infection not responding to first or second line therapy	Seek advice from a medical microbiologist
Antibiotics for a further episode of *C.difficile* infection within 12 weeks of symptom resolution (relapse)	Seek advice from a medical microbiologist
Antibiotics for a further episode of *C.difficile* more than 12 weeks after symptom resolution (recurrence)	Mild/moderate vancomycin 125mg PO 6hrly for 10 days Severe Seek advice from a medical microbiologist

Other therapies

Antimicrobials should not be used to prevent *C.difficile* infection and probiotics not to be used routinely to prevent *C.difficile*. Bezlotoxumab is not recommended in the prevention of recurrence of *C.difficile* infection.

Referral for faecal microbiota transplant could be considered for recurrent *C.difficile* infection in adults who have had two or more previous episodes of *C.difficile* infection and not responded to antibiotics – please discuss with an Infection Specialist (medical microbiology).

4.2 Guidelines for the Antimicrobial Management of Patients with Methicillin Resistant Staphylococcus aureus (MRSA) Infection

See also the NBT Infection Control MRSA policy

Introduction

In North Bristol NHS Trust, MRSA infection is relatively rare – only patients known to be MRSA colonised or those with prior infection require empiric therapy.

Antibiotics used in the therapy of MRSA

Vancomycin (see section 6.3 for dosing) for IV therapy

Doxycycline (100mg BD PO) for oral therapy

Duration of therapy

For non severe infection, 5 days of therapy is satisfactory. For cellulitis 5-14 days therapy may be required depending on severity and response rates. A bacteraemia with no evidence of deep infection, infective endocarditis or prosthesis associated infection should be treated for 14 days with vancomycin, particularly if IV line associated and the line is removed. For complicated bacteraemia, a longer duration will be required.

If there is doubt about therapy duration, discuss with a medical microbiologist.

4.3 Invasive Fungal Infection

Please discuss all potential invasive fungal infections with a Medical Microbiologist.

5.1 ANTIBIOTIC GUIDELINES FOR NEUROSURGERY

5.1.2 Protocol for patients whose EVDs are to be removed or who are to undergo shunt implantation

Three days before removal of an EVD/shunt implantation obtain a sample of CSF and submit to the Microbiology Department for Gram's film and culture.

Instil vancomycin 10mg and gentamicin 3mg (15mg and 4mg respectively for patients with very large ventricles) into the ventricles after the sample has been obtained.

The frequency of subsequent doses will depend on the volume of CSF drainage and must be assessed daily, at 24-hour intervals after the previous dose.

<50 mL	no further doses (except 1 intraoperative dose at the time of shunt implantation)
50-100 mL daily	a second dose on the third day (+ 1 intraoperative dose at the time of shunt implantation)
100-150 mL daily	a daily dose (+ 1 intraoperative dose at the time of shunt implantation)
150-250 mL daily	daily doses of vancomycin 15mg and gentamicin 4mg (+ 1 intraoperative dose at the time of shunt implantation)

NB For patients undergoing shunt implantation administer systemic prophylaxis according to prophylaxis guidelines (page 27)

Before EVD removal

If the final report on the sample of CSF (usually available 3 days after it was obtained) confirms that it is sterile remove the EVD.

If a Gram's stain of the sample of CSF (performed on receipt of the specimen) indicates the presence of bacteria, send a second sample for confirmation and continue vancomycin ± gentamicin (depending on isolate) for a further 4 days (5 days in total) according to the dosing frequency described above and then remove the EVD. If the Gram's stain suggests that the sample is sterile, but culture yields a bacterium (usually after 2-3 days) send a second sample for confirmation and continue the antibiotic(s) for a further 2-3 days (5 days in total) according to the dosing frequency described above and then remove the EVD.

Before shunting

If the CSF is reported to be sterile (usually 3 days after it was obtained) no further doses should be given following implantation of the shunt.

If a Gram's stain of the CSF indicates infection, send a second sample for confirmation. The consultant can then decide whether to continue giving the antibiotic(s) according to the dosing frequency described above until the shunt has been implanted and then to give vancomycin ± gentamicin (depending on the bacterium) via an Ommaya reservoir **daily** for 5-7 days following implantation **OR** to delay shunting until the patient has received vancomycin ± gentamicin (depending on the bacterium) for a total of 5 days according to the dosing frequency described above.

If the Gram's stain suggests that the sample is sterile, but culture yields a bacterium (usually after 2-3 days) send a second sample for confirmation. The consultant can then decide whether to give

vancomycin ± gentamicin (depending on the bacterium) via an Ommaya reservoir **daily** for 5-7 days following implantation **OR** to delay shunting until the patient has received vancomycin ± gentamicin (depending on the bacterium) for a total of 5 days according to the dosing frequency described above.

5.1.3 CSF shunt infections

Treatment is administered on an individual basis according to recommendations provided by the Medical Microbiologists.

5.1.4 Pyrexia in patients with blood in the ventricles

Patients with blood in their ventricles often have fevers. In such patients **who have no obvious foci of infection**, the initial investigation should be a CRP. If this is <100, no further investigations or empirical antibiotic treatment is indicated as the fever is almost certainly 'central' in origin. If the CRP is >100, an infection screen should be undertaken and, where appropriate, empirical therapy started.

5.1.5 Treatment of External Ventricular Drain (EVD) associated ventriculitis

If a Gram's film or culture result suggests that a patient has EVD-associated ventriculitis a second sample should be obtained as soon as possible. The diagnosis is confirmed by isolation of the same bacterium from two consecutive specimens. However, antibiotic(s) can be initiated immediately after the second sample has been obtained. If this sample is subsequently shown to be sterile, treatment should be discontinued.

The antibiotic(s) given will depend on the nature and susceptibility of the pathogen. Usually only vancomycin and gentamicin are administered by the intraventricular route, and patients will receive one or both of these drugs. A minority of patients will also require systemic therapy.

Please consult the table below for guidance on appropriate dosing regimens. Treatment will be guided by a Medical Microbiologist on an individual patient basis.

NB It is clear that the criteria for choosing the dosages of vancomycin and gentamicin are largely subjective. However, if these regimens are followed, the likelihood of either underdosing or, owing to the excellent safety record of the drugs, overdosing will be minimal; toxicity associated with intraventricular administration of vancomycin has never been reported. It will be exceptional for a patient to receive >25mg of vancomycin or >5mg of gentamicin.

5.1.6 Postoperative patients with the clinical signs and/or symptoms of meningitis

A small percentage of neurosurgical patients will, in the postoperative period, develop signs and/or symptoms consistent with a diagnosis of meningitis; this may present one month or more after the surgery. In the majority (70%) of such cases, the meningitis is not of infective aetiology. However, there are no clinical criteria which can be used to reliably differentiate between those who do and those who do not have bacterial meningitis.

Investigations: Examination of CSF, including glucose concentration; simultaneous blood glucose determination; full blood count and CRP.

Management: Commence treatment with ceftriaxone 2g BD IV. If no bacterium is isolated after 3 days of incubation and the patient has made a rapid clinical response (usually within 24 h), discontinue treatment.

If a bacterium which is considered to be a true pathogen is isolated, further treatment should be discussed with a Medical Microbiologist.

5.1.7 Postoperative wound infections

The results of culture of the wound, if available, should be used to guide antibiotic treatment. If the results are not available and empirical therapy is required, flucloxacillin (1g QDS IV/ 500mg QDS PO), or clindamycin 600mg QDS IV / 300mg PO in patients who are allergic to penicillin, would be appropriate.

5.1.8 Brain abscess

Empirical therapy of patients with brain abscesses should be based on the site of the abscess and predisposing infectious processes, if they can be identified; an urgent Gram stain of pus obtained at the time of surgery might also be helpful. CRP should be used to monitor response to treatment.

Abscesses (usually frontal) which are sinugenic, odontogenic or of unknown origin:
ceftriaxone 2g BD IV + metronidazole 500mg TDS IV

Abscesses (usually temporal) which are otogenic:
ceftazidime 2g TDS IV + amoxicillin 1g TDS IV + metronidazole 500mg TDS IV

5.1.9 Subdural empyema

Empirical therapy of patients with subdural empyemata should be based on predisposing infectious processes and a Gram stain of pus obtained at the time of surgery. CRP should be used to monitor response to treatment.

Empirical antibiotic treatment: ceftriaxone 2g OD IV + metronidazole 500mg TDS IV

5.1.10 Antibiotic treatment regimens for patients with EVD-associated ventriculitis

Dosage according to CSF volume of distribution (baseline dosage)

Antibiotic	**<normal**	**normal**	**moderately >normal**	**markedly >normal**
vancomycin	5 mg	10 mg	15 mg	20 mg
gentamicin	2 mg	3 mg	4 mg	5 mg

Frequency of baseline dosage (according to CSF drainage since previous dose)

Antibiotic	**<50 ml over 3 days**	**50-100 ml over 2 days**	**100-150 ml in 24 hours**	**>150 ml in 24 hours**
vancomycin	every third day	alternate days	daily	daily + 5 mg for each 50 ml, or part thereof, >150 ml
gentamicin	every third day	alternate days	daily	daily + 1 mg for each 50 ml, or part thereof, >150 ml

5.2 Empirical antibiotic therapy for Burn patients with A) Burn wound infection and B) presumed septic shock

A. Burn Wound Infection

Time since injury occurred	Previous antibiotic therapy within the last 14 days	Treatment
≤5 days	No	flucloxacillin 2g QDS IV Penicillin allergy: clindamycin 600mg QDS IV
	Yes	amoxicillin 1g TDS IV + co-trimoxazole 960mg BD IV Penicillin allergy: co-trimoxazole 960mg BD IV + IV vancomycin
6-9 days	No	amoxicillin 1g TDS IV + co-trimoxazole 960mg BD IV Penicillin allergy: co-trimoxazole 960mg BD IV + IV vancomycin
	Yes	piperacillin/tazobactam 4.5g TDS IV Penicillin allergy (non-type 1, non-severe): ceftazidime 2g TDS IV plus IV vancomycin Penicillin allergy (type 1 allergy/severe reaction): ciprofloxacin 500mg BD PO/400mg BD IV+ IV vancomycin. Provide MHRA patient information leaflet about quinolone side effects
≥10 days	Yes or No	piperacillin/tazobactam 4.5g TDS IV or discuss with medical microbiology Penicillin allergy (non-type 1, non-severe): ceftazidime 2g TDS IV plus IV vancomycin Penicillin allergy (type 1 allergy/severe reaction): ciprofloxacin 500mg BD PO/400mg BD IV+ IV vancomycin. Provide MHRA patient information leaflet about quinolone side effects

If a patient with clinical infection is:

- colonised with MRSA - add vancomycin
- colonised with *Pseudomonas aeruginosa* – use piperacillin/tazobactam at a dose of 4.5g QDS IV. If using ciprofloxacin as part of the 'penicillin allergy' regimens above, use a dose of 750mg BD PO/400mg TDS IV. Provide MHRA patient information leaflet about quinolone side effects
- colonised with an MDR Gram-negative rod or has been transferred from another hospital which has a high incidence of MDR organisms – consultant a Medical Microbiologist
  Duration of therapy: 5 days if pathogen isolated from burn wound; 3 days if no pathogen isolated. Review therapy at 48hrs.

1. Please note that patients with severe burns may develop pyrexia in the first few days after the injury even without sepsis and that cleaning of the burn in theatre can result in pyrexia and tachycardia that is transient in the first few hours after surgery. If any concerns about sepsis, a full review is mandated including history and examination. There should be a low threshold for re-examination of the burn wound for signs of infection.

B. Sepsis in a burns patient

The American Burn Association diagnosis of sepsis in burns patient is made after establishing the existence of an infection (documented by clinical response to antibiotics, pathological analysis of tissues from the wound or positive cultures) and at least three of the following criteria:

1. Temperature >39° or <36.5°C
2. Progressive tachycardia (>110 beats per min)
3. Progressive tachypnea (>25 breaths per minute not ventilated or minute ventilation >12l/min ventilated)
4. Thrombocytopenia <100 $x10^9$/l (will not apply until 3 days after initial resuscitation)
5. Hyperglycaemia, in the absence of pre-existing diabetes mellitus (untreated plasma glucose >11 mmol/l or >7 units of insulin/h intravenous drip or significant resistance to insulin, >25% increase in insulin requirement over 24h)
6. Inability to continue enteral feedings >24 h (abdominal distension or high gastric residuals, residuals two times feeding rate or uncontrollable diarrhoea, >2500 ml/day).

If any concerns about sepsis, a full review is mandated including history and examination. There should be a low threshold for re-examination of the burn wound for signs of infection. Consider swabbing the wound for microbiological assessment. All potential burn wound sepsis should be discussed with the burns consultant on call.

In addition to patients who fit the above criteria for sepsis, this antibiotic protocol should also be used in patients who are at high risk of sepsis including:

- Burns patients who are in ITU with inhalational injury
- Immunosuppressed patients with large open wounds

The antimicrobial therapy is:

Piperacillin/tazobactam 4.5g QDS IV

If patient is:

- colonised with MRSA - add vancomycin
- colonised with an MDR Gram-negative rod or has been transferred from another hospital which has a high incidence of MDR organisms – consult a Medical Microbiologist
- penicillin allergic - consult a Medical Microbiologist.

Patients should be deescalated to narrow spectrum therapy when culture results are available (48hr review).

5.2.2 Plastic surgery

		Penicillin allergy	**comments**
Cellulitis/ erysipelas	Flucloxacillin 2g QDS IV for 5-14 days oral switch: 500mg QDS	Clindamycin 600mg QDS IV for 5-14 days Oral switch: 300mg QDS	
Limb Abscess	Flucloxacillin 2g QDS IV for 7-14 days oral switch: 500mg QDS	Clindamycin 600mg QDS IV for 7-14 days Oral switch: 300mg QDS	

Animal and human bites	Co- amoxiclav 1.2g IV TDS or 625mg PO TDS for 5 days	Clindamycin 300mg PO (450mg IV) QDS +/- Ciprofloxacin* 750mg BD PO for 7 days * Provide MHRA patient information leaflet about quinolone side effects **Discuss with a Microbiologist.**	
Wound infection following clean surgery	Flucloxacillin 2g QDS IV for 5 days oral switch: 500mg QDS	Clindamycin 450mg QDS IV for 5 days Oral switch: 300mg QDS	Send MRSA Swabs
Cellulitis at a cannula site	Flucloxacillin 2g QDS IV for 5 days oral switch: 500mg QDS	Clindamycin 450mg QDS IV for 5 days Oral switch: 300mg QDS	
Cellulitis in a current injecting drug user	Flucloxacillin 2g QDS IV for 5 days oral switch: 500mg QDS	Clindamycin 450mg QDS IV for 5 days Oral switch: 300mg QDS	If known to be colonised with MRSA give vancomycin (see section 6.3 for dosing)
Mastitis and breast abscesses	Flucloxacillin 2g QDS IV for 5 days oral switch: 500mg QDS	Clindamycin 450mg QDS IV for 5 days Oral switch: 300mg QDS	
Necrotising fasciitis	Piperacillin-tazobactam 4.5g IV QDS plus clindamycin 600mg IV QDS If the patient is colonised with MRSA, has risk factors for MRSA, or is an IVDU – add vancomycin (see section 6.2 for dosing)	penicillin allergy – consult a Medical Microbiologist	Discuss treatment with a Medical Microbiologist as soon as diagnosis is made, early appropriate therapy is imperative. Consider the use of IVIG, especially in patients in whom Group A streptococcal infection seems likely.
Perianal infection	Co-trimoxazole 960mg BD IV and metronidazole 500mg TDS IV for 5 days Oral switch: co-trimoxazole 960mg BD + metronidazole 400mg TDS		

5.3 Richard Bright Renal Unit. Use of Antibiotics

Advice on renal dose adjustment for commonly prescribed antimicrobial agents is available in Appendix B.

Haemodialysis	• Haemodialysis vascular access exit site colonisation and infection – see renal unit protocol for MRSA and MSSA screening and treatment: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7351&SearchId=0 • Suspected bacteraemia related to haemodialysis vascular access – give empirical vancomycin IV using the renal unit protocol for vancomycin in haemodialysis patients https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7412&SearchId=0 • Haemodialysis line lock policies: ○ Gentamicin and heparin: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7409&SearchId=0 ○ Citralock: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7409&SearchId=0
Peritoneal dialysis	• See renal unit protocol for treatment of PD peritonitis and exit site infections: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7421&SearchId=0
Transplant	• Guidance on prevention of infection post kidney transplant is available in the renal transplant protocol https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7555&SearchId=0 • Prophylaxis and treatment of CMV infection post kidney transplantation: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=16518&SearchId=0
Suspected gram-negative bacteraemia (from urinary tract or gastrointestinal disease)	• **First line:** piperacillin/tazobactam 4.5g 8 hourly IV, adjusted if necessary for renal function • **Penicillin allergy:** Discuss with microbiology
Polycystic kidney disease cyst infection	• See renal unit guidelines for ADPKD cyst infection diagnosis and management: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7365&SearchId=0
Hepatitis B	• Hepatitis B vaccination in chronic kidney disease: https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7353&SearchId=0 • Guidance on prevention of hepatitis B infection post kidney transplant is available in the renal transplant protocol https://link.nbt.nhs.uk/Interact/Pages/Content/Document.aspx?id=7555&SearchId=0

5.4. Hot Orthopaedics and Trauma Post Operative Wound Infection

Most post-operative wound infections in emergency related Orthopaedic Surgery in patients without prosthetic joints are cause by *S. aureus*. The drug of choice is flucloxacillin. If the patient is known to be MRSA-positive, the drug of choice is vancomycin (see section 6.2 for dosing). The regimen should be altered, if appropriate, in the light of culture results. Infections in patients with prosthetic joint infection are more complex, and these guidelines do not apply in these situations.

5.4.1 Septic arthritis

The predominant aetiological agent is *S. aureus*, followed by β-haemolytic streptococci. However, as almost any bacterium can be implicated, it is important to identify the pathogen.

Investigations:	blood cultures x 2, joint aspirate (including urgent Gram stain), CRP (and repeat every 5-7 days to monitor response to therapy)
Empirical therapy:	flucloxacillin 2g QDS IV otherwise, according to Gram stain results of joint aspirate
Definitive therapy: *S. aureus*	 flucloxacillin 2g QDS IV
Duration:	4 weeks in total (5-7 days IV, remainder PO)

5.4.2 Acute Osteomyelitis – not related to prosthetic joints

The predominant aetiological agent is *S. aureus.* However, the range of potential pathogens is extensive. Elderly patients in particular may be infected by unusual organisms. In patients (usually diabetics) with infected foot ulcers, multiple bacterial species may be implicated. It is **ESSENTIAL** therefore to identify the microbiological cause(s).

Investigations:	bone biopsy/aspirate (including urgent Gram stain), blood culture x 2, CRP (and repeat every 5-7 days to monitor response to therapy) Do not rely on the results of superficial swabs of ulcers to identify the cause(s) of the bone infection
Empirical therapy:	flucloxacillin 2g QDS IV
Definitive therapy: *S. aureus* other pathogens	 flucloxacillin 2g QDS IV discuss with Medical Microbiologist
Duration:	minimum 6 weeks in total (5-10 days IV, remainder PO)

5.4.3 Acute infections in patients with metalwork *in situ*, but where the metalwork cannot be removed until the fracture has united

seek advice from a Medical Microbiologist
NB. It must be assumed that the bone is infected

5.4.4 Open Fractures

First line: Co-amoxiclav 1.2g TDS IV

In patients with a penicillin allergy: Teicoplanin (see section 6.4 for dosing) IV BD x 3 doses then OD + gentamicin IV (see section 6.1 for dosing)

Therapy should continue for a maximum of 72 hours or until soft tissue closure, whichever is sooner.

Give IV antibiotics ASAP: time to antibiotics affects long term outcome in open fractures.

5.4.5 Spinal abscesses/infection

All patients with a proven or presumed spinal infection should be discussed with Microbiology.

5.5. Obstetrics and Gynaecology

The following relevant guidelines can be found on the Maternity homepage:

http://sharepoint/sites/wch/teamsite/maternity/GuidelinesHomepage/AZList/Forms/AZ.aspx

- Group B Streptococcal (GBS) Care in pregnancy and labour
- Sepsis (and empirical treatment of common perinatal infections)
- UTI in Pregnancy
- Management of Pre Term pre labour rupture of membranes 24-37 Weeks

5.5.1 Pelvic Inflammatory Disease

Outpatient in mild/moderate PID has equivalent outcomes to inpatient treatment. However antibiotics should be started as soon as PID is suspected as delay may increase the severity of infection and the risk of long term sequelae.

The BASHH recommended regimes for outpatient treatment of PID are:

- ofloxacin 400mg BD PO + metronidazole 400mg BD PO for 14 days.

OR

- Stat dose of ceftriaxone 1000mg IM followed by doxycyline 100mg BD PO + metronidazole 400mg BD PO for 14 days.

Ofloxacin should be avoided in patients at high risk of gonococcal infection (e.g. partner has GC) and metronidazole may be discontinued in patients with mild/moderate PID if they are intolerant.

Inpatient treatment or Hospital at Home support is indicated in patients with severe PID, pregnant patients, non-response or intolerance of oral treatment, suspected tubo-ovarian abscess or where urgent surgical treatment may be necessary.

The BASHH recommended regimes for inpatient treatment of PID are:

- ceftriaxone 2g OD IV + doxycycline 100mg BD PO (oral switch: doxycycline 100mg BD PO + metronidazole 400mg BD PO) for 14 days total.

OR

- clindamycin 900mg TDS IV + gentamicin IV (see section 6.1 for dosing), followed by either:
  - clindamycin 450mg QDS PO to complete 14 day course
  - doxycycline 100mg BD PO + metronidazole 400mg BD PO to complete 14 day course.

IV antibiotics should be continued until 24 hours after clinical improvement and followed by oral therapy.

6. DOSING OF GENTAMICIN, AMIKACIN AND VANCOMYCIN

Antibiotic Assays – Gentamicin, Amikacin and Vancomycin

To ensure the medical microbiologist can provide timely and accurate advice on antibiotic assays, the following data is required:-

- antibiotic to be assayed
- last dose (mg)
- when last dose given (hour, date)
- whether dose pre/post dose level
- the dose size (mg) and the time of dose (hour, date) and time of assay (hour, date)

Failure to provide this information may result in the assay not being performed.

6.1. Gentamicin

(a) Therapy

As gentamicin does not penetrate into adipose tissue significantly, **obese patients (BMI ≥30kg/m^2) should be dosed based on their ideal body weight** which is calculated as:

Male: ideal body weight = 50 + (2.3 x height in inches over 5ft)
Female: ideal body weight = 45.5 + (2.3 x height in inches over 5ft)

Creatinine clearance	gentamicin dose	dose frequency
>80ml/min	7mg/kg	24 hours
40-80ml/min	5mg/kg	24 hours
20-40ml/min	5mg/kg	48 hours
<20ml/min (discuss use with a medical microbiologist)	5mg/kg	measure level at 48h and await the result before giving next dose

The maximum dose of gentamicin should not exceed **560mg** daily.

Creatinine clearance should be used instead of eGFR. This can be calculated using the Cockcroft-Gault formula which can be found here or the gentamicin calculator on the Microbiology homepage.

A pre-dose gentamicin level should be measured before the second dose and should be ≤1mg/L. Take pre-dose assays immediately before the dose is due – do not wait for the result before giving the next dose unless advised.

Provided the pre-dose level before the second dose is ≤1mg/L, then gentamicin should be re-assayed twice in the following week. Renal function should be monitored **daily** while a patient is on gentamicin.

If the pre-dose level is >1mg/L, dosing modification or use of an alternative agent may be required. This should be discussed with a medical microbiologist.

Once-a-day dosing regimens have only been validated for patients with normal renal function (creatinine clearance >80ml/min) and therefore some caution is required in patients with renal impairment. Once-daily dosing is not appropriate for treating endocarditis.

Gentamicin is excreted by the kidney, and accumulation may result in nephrotoxicity and ototoxicity. Those at special risk include the elderly, hypotensive patients and those with existing renal impairment. Prescribers who have concerns about the dose to use and its frequency should discuss with a medical microbiologist or infection pharmacist.

No patient should receive gentamicin for more than 7 days without clinical advice from a medical microbiologist.
When gentamicin is being used as monotherapy in the therapy of aerobic Gram-negative rods (coliforms or Pseudomonas spp), a peak concentration 1hr after the dose should be taken. This should be ≥7mg/L.

(b) Prophylaxis

Where gentamicin is used as prophylaxis (see Section 3.2), then the following guide should be used.

creatine clearance (eGFR)	Dose (depending on procedure)	
>80ml/min	5mg/kg	3mg/kg
40-80ml/min	3.5mg/kg	2mg/kg
<40ml/min	2mg/kg	1mg/kg

- 5mg/kg dose is used for prophylaxis in orthopaedic surgery, except lower limb amputation
- obese patient BMI ≥30kg/m^2, use ideal body weight (see above) to calculate dose

6.2. Amikacin

As amikacin does not penetrate into adipose tissue significantly, **obese patients (BMI ≥30) should be dosed based on their ideal body weight** which is calculated as:-

Male: ideal body weight = 50 + (2.3 x height in inches over 5ft)
Female: ideal body weight = 45.5 + (2.3 x height in inches over 5ft)

Creatinine clearance	amikacin dose	dose frequency
>80ml/min	15mg/kg	24 hours
40-80ml/min	10mg/kg	24 hours
20-40ml/min	10mg/kg	48 hours
<20ml/min (discuss use with a medical microbiologist)	10mg/kg	measure level at 48h and await the result before giving next dose

Creatinine clearance should be used instead of eGFR. This can be calculated using the Cockcroft-Gault formula which can be found here.

A pre-dose amikacin level should be measured before the second dose and should be ≤5mg/L. Take pre-dose assays immediately before the dose is due – do not wait for the result before giving the next dose unless advised.

Provided the pre-dose level before the second dose is ≤5mg/L, then amikacin should be re-assayed twice in the following week. Renal function should be monitored **daily** while a patient is on amikacin.

If the pre-dose level is >5mg/L, dosing modification or use of an alternative agent may be required. This should be discussed with a medical microbiologist.

Once-a-day dosing regimens have only been validated for patients with normal renal function (creatinine clearance >80ml/min) and therefore some caution is required in patients with renal impairment. Amikacin should not be used to treat endocarditis.

Amikacin is excreted by the kidney, and accumulation may result in nephrotoxicity and ototoxicity. Those at special risk include the elderly, hypotensive patients and those with existing renal impairment. Prescribers who have concerns about the dose to use and its frequency should discuss with a medical microbiologist or infection pharmacist.

No patient should receive amikacin for more than 7 days without clinical advice from a medical microbiologist.

Amikacin is only used in these guidelines for the therapy of hospital acquired complicated UTI and peak concentrations assays are not required.

6.3 Vancomycin

Vancomycin is dosed twice a day and serum levels are monitored to reduce the risk of significant accumulation and nephrotoxicity. Vancomycin is administered in a volume of 100-250ml by slow infusion (10mg/min) to avoid red man syndrome. Vancomycin is excreted almost entirely via the kidney.

Vancomycin pre-dose levels should be measured at the 3rd or 4th dose as convenient. Pre-dose assays should be taken immediately before the dose is given. Do not delay the dose until the result is available. The pre-dose vancomycin level should be in the range 5-15mg/L. If this is the case, a further pre-dose should be measured once per week plus a serum creatinine over the duration of therapy.

In obese patients, total body weight should be used to determine initial dosing using a dose of 15mg/kg every 12 hrs.

The following dosing guide should be used:-

creatinine clearance	vancomycin dose	dose frequency
>80ml/min	1000mg	12hrly
40-80ml/min	750mg	12hrly
20-40ml/min	500mg	12hrly
<20ml/min*	1000mg	measure level at 48h and await the result before giving the next dose

eGFR is normally an acceptable estimate of creatinine clearance. In patients with extremes of bodyweight or who are over 75 years old, creatinine clearance should be calculated using the Cockcroft-Gault formula which can be found here.

*For patients with creatinine clearances of <20ml/min not under the care of a renal physician, please discuss the dosing with a medical microbiologist or infection pharmacist.

Alternatively, if the serum creatinine is <110µmol/L, then the following guide can be simpler based on age.

Age (years)	vancomycin dose	Dose frequency
<60	1000mg	12hrly
60-75	750mg	12hrly
>75	500mg	12hrly

6.4. Teicoplanin

Doses are weight based. Please use **actual body weight**

Treatment of non-deep seated infections (e.g. skin and soft tissue infections)

Actual body weight (kg)	Loading dose (6mg/kg)	Maintenance dose (6mg/kg)
<45	6mg/kg IV every 12 hours for 3 doses	6mg/kg IV once daily
45-74	400mg IV every 12 hours for 3 doses	400mg IV once daily
75-109	600mg IV every 12 hours for 3 doses	600mg IV once daily
110-144	800mg IV every 12 hours for 3 doses	800mg IV once daily
≥145	1000mg IV every 12 hours for 3 doses	1000mg IV once daily

Treatment of deep seated infections (e.g. bone and joint infections, endocarditis)

Actual body weight (kg)	Loading dose (12mg/kg)	Maintenance dose (12mg/kg)
<45	12mg/kg IV every 12 hours for 3 doses	12mg/kg IV once daily
45-55	600mg IV every 12 hours for 3 doses	600mg IV once daily
56-74	800mg IV every 12 hours for 3 doses	800mg IV once daily
75-90	1000mg IV every 12 hours for 3 doses	1000mg IV once daily
91-105	1200mg IV every 12 hours for 3 doses	1200mg IV once daily
106-125	1400mg IV every 12 hours for 3 doses	1400mg IV once daily
126-140	1600mg IV every 12 hours for 3 doses	1600mg IV once daily
≥141	1800mg IV every 12 hours for 3 doses	1800mg IV once daily

Dose adjustment in renal impairment

Creatinine clearance (ml/min)	Dose adjustment
>80	Normal regime (see table above)
30-80	Normal dosing regime on days 1-4 (see table above), then give normal maintenance dose every 48 hours
<30 and renal replacement therapy	Normal dosing regime on days 1-4 (see table above), then give normal maintenance dose every 72 hours

Therapeutic drug monitoring

There is minimal evidence for dose-related toxicity. Monitoring of levels is performed to ensure that therapeutic levels are achieved.

Levels should be taken immediately pre-dose. Do not delay the dose until the result is available.

Timing of initial sample: Immediately pre-dose on day 4

Timing of subsequent samples: Re-assay after 6-8 days or as directed by microbiology

Target pre-dose concentrations:

Indication	Target pre-dose concentration
Skin and soft tissue infection	15-30mg/L
Bone and Joint infection	20-40mg/L
Infective endocarditis	30-40mg/L

7. Assessment of penicillin allergy

Many patients claim to be allergic to penicillin and a significant proportion of these are incorrectly labelled as "penicillin allergic" either on the basis of symptoms reflecting drug side effects (i.e. nausea or diarrhoea) or disease symptoms (cough). This is often related to inadequate history taking at presentation. Incorrect labelling as penicillin allergic may have significant adverse effects on future antibiotic therapy leading to less effective or more toxic antimicrobial therapy. A thorough, reliable history (from patient, family or General Practitioner) is paramount in identifying those with true allergy, be it mild or severe. The exact nature of the drug allergy should be documented on the prescription sheet and patient's notes.

Characteristics	Type 1 immediate hypersensitivity reactions (anaphylactoid)	Non-type 1 reactions (Type II-IV: idiosyncratic)
Timing onset	up to 4 hours from exposure	>4 hr from exposure
Clinical signs	anaphylaxis laryngeal oedema wheezing/bronchospasm angioedema urticaria/pruritus diffuse erythema	maculopapular rash morbilliform rash reduced RBC, platelets drug fevers contact dermatitis
Classification	severe penicillin and beta-lactam allergy	non-severe penicillin allergy
Drugs to <u>AVOID</u>	avoid <u>ALL</u> penicillins avoid <u>ALL</u> cephalosporins avoid <u>ALL</u> carbapenems and monobactams Examples to <u>AVOID</u> include (please note this list is not exhaustive) amoxicillin co-amoxiclav benzyl and phenoxy methyl penicillin flucloxacillin piperacillin-tazobactam (Tazocin) Ticarcillin-clavulanic acid pivmecillinam cefotaxime ceftriaxone	avoid <u>ALL</u> penicillins Examples to <u>AVOID</u> include (please note this list is not exhaustive) amoxicillin co-amoxiclav benzyl and phenoxy methyl penicillin flucloxacillin piperacillin-tazobactam (Tazocin) ticarcillin-clavulanic acid pivmecillinam

	cefuroxime ceftazidime +/- avibactam ceftolozane-tazobactam ceftaroline meropenem ertapenem aztreonam	
Drugs to use with **CAUTION**		**CAUTION** with cephalosporins, carbapenems and monobactams

Please seek advice from an Infection Specialist (Medical Microbiology) for alternative therapies.

8. REFERENCES AND GLOSSARY

British National Formulary

British National Formulary for Children

BSR & BHPR, BOA, RCGP and BSAC guidelines for management of the hot swollen joint in adults. Rheumatology 2006, 45, 1039-41, or www.bsac.org.uk/resource_library.cfm

Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy. www.bsac.org.uk/resource_library.cfm

Guidelines for the prophylaxis and treatment of MRSA infection
www.bsac.org.uk/resource_library.cfm

National Institute for Clinical Excellence. Chronic obstructive pulmonary diseases. Management of COPD in adults in primary and secondary care.
www.nice.org.uk/pdf/CG012_niceguideline.pdf

British Thoracic Society. Guidelines for the Management of Community acquired pneumonia in adults. Thorax 2001; 56 (Suppl IV) or www.brit-thoracic.org.uk/bts_guidelines_pneumonia_html

Guidelines for Management of CAP in adults, 2004 update. www.brit-thoracic.org.uk

Glossary

BNF	British National Formulary
CAP	Community acquired pneumonia
CMV	Cytomegalovirus
CNS	Central Nervous System
CPE	Carbapenemase producing Enterobacterales
CRP	C-Reactive Protein
CSF	Cerebrospinal fluid
CSU	Catheter stream urine
CXR	Chest X-ray
ESBL	Extended Spectrum Beta-Lactamase
EVD	Extra-ventricular drain
FBC	Full blood count
HAP	Hospital acquired pneumonia
HCAI	Healthcare Associated Infection
HSV	Herpes Simplex virus
IV	Intravenous
MC&S	Microscopy, Culture and Sensitivities
MDR	Multi-Drug Resistant
MRSA	Methicillin Resistance Staphylococcus Aureus
MSU	Mid-stream urine
OPAT	Outpatient Parenteral Antimicrobial Therapy
TDM	Therapeutic Drug Monitoring
VRE	Vancomycin Resistant Enterococci
VZV	Varicella Zoster virus

Appendix A Guideline for Vaccinations and Prophylactic Antibiotics required for Adult Patients Undergoing Emergency or Elective Splenectomy

Patients who have had a splenectomy are at risk of overwhelming infection from certain microorganisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type B and *Neisseria meningitidis*. These guidelines also apply to patients with non-functioning spleens.

Vaccinations

The Department of Health recommends the following vaccinations in patients who have had or are going to have a splenectomy.

- **Meningococcal MenB and MenACWY**
- **Pneumococcal (23-valent)**
- **Influenza**

Where possible, vaccines should be administered at least two weeks prior to **elective surgery**. Ideally this should be carried out by the GP prior to the hospital admission. If patient is not vaccinated beforehand then surgery should not be delayed.

In the case of **emergency splenectomy** current guidance is to wait 2 weeks before giving vaccinations. However immunisation should not be delayed if this is likely to result in failure to vaccinate. The clinician may prefer to vaccinate the patient before discharge to ensure that it has been done.

Schedule- Applies to adults only regardless of previous vaccination status

Vaccine	Timing
Pneumococcal polysaccharide Vaccine (PPV)	**Elective splenectomy**- GP to vaccinate at least 2 weeks prior to admission. **Emergency splenectomy**- 2 weeks post- surgery or before discharge. Booster dose every 5 years in asplenic patients
Meningitis B Vaccine (Bexsero)	**Elective splenectomy –** GP to vaccinate prior to admission. Two doses needed 1 month apart. The second dose should be at least 2 weeks prior to admission. **Emergency splenectomy –** First dose 2 weeks post-surgery or prior to discharge. Second dose one month after initial vaccines.
MenACWY conjugate	**One month after initial vaccines** **Inform GP to give**
Seasonal Influenza	**Inform GP to give as soon as practical. Should be given annually.**

DETAILS OF VACCINATIONS GIVEN MUST BE CLEARLY DOCUMENTED IN THE PATIENTS NOTES AND ON THE DISCHARGE LETTER. PLEASE INFORM GP TO FOLLOW UP ON VACCINES NOT GIVEN.

Cautions

Vaccinations should be delayed if the patient has signs of significant febrile illness.

Please seek specialist advice if patient undergoing chemotherapy or radiotherapy as the pneumococcal vaccine may have to be delayed.
Patients with immunosuppression or HIV may not make a full antibody response to pneumococcal vaccine. Please seek specialist advice.

Prophylactic antibiotics

- Phenoxymethylpenicillin 250mg PO BD or amoxicillin 500mg PO BD
- Erythromycin 500mg PO BD in penicillin allergic patients

Lifelong prophylactic antibiotics should be offered to patients considered at continued high risk of pneumococcal infection. See current British Journal of Haematology guidelines for further information. Antibiotic prophylaxis is **essential** in the first 2 years after the operation.

http://www.bcshguidelines.com/documents/Review_of_guidelines_absent_or_dysfunctional_spleen_2012.pdf

Additional points

Patients are to be advised to seek medical attention immediately if they are ill. Especially if they experience symptoms such as fever, sore throat severe headache or abdominal pain.

Patients are to be advised to get treatment for any bites (especially dog)

Patients are to be advised to seek advice on malaria prophylaxis and extra vaccinations if travelling abroad.

All Patients must be given a copy of "Splenectomy information for patients" – also available from pharmacy.

References

Davies JM, Lewis MPN, Wimperis J, Rafi I, Ladhani S, Bolton-Maggs PHB. Review of guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen: Prepared on behalf of the BCSH by a Working Party of the Haemato-Oncology task Force. British Journal of Haematology,2011; 155: 308-317.
http://www.bcshguidelines.com/documents/Review_of_guidelines_absent_or_dysfunctional_spleen_2012.pdf

Department of Health. Immunisation Against Infectious Diseases– "The Green Book". Updated version available online: https://www.gov.uk/government/publications/immunisation-of-individuals-with-underlying-medical-conditions-the-green-book-chapter-7

Splenectomy information for patients. Department of Health .
https://www.gov.uk/government/publications/splenectomy-leaflet-and-card

BNF online: https://bnf.nice.org.uk/

Appendix B Guidelines for antimicrobial dosing in patients with impaired renal function

These guidelines aim to provide information on suitable dose adjustments for frequently prescribed antimicrobials in hospital inpatients with impaired renal function. These guidelines do not aim to provide information on all antimicrobials and complex patients should be discussed with microbiology and/or a member of the renal pharmacy team. Information produced by manufacturers on antimicrobials not included in this document can be found online at **http://emc.medicines.org.uk** or alternatively individual cases can be discussed with a member of the renal pharmacy team.

Recommendations are based on the patient's current creatinine clearance (CrCl), which is used as an estimate of renal function. eGFR is normally an acceptable estimate of renal function for drug dosing, however exceptions to the use of eGFR include antimicrobials with a narrow therapeutic index, elderly patients and patients at extremes of bodyweight In these circumstances calculation of CrCl using the Cockroft and Gault formula is recommended. Caution must be used when dosing patients with unstable renal function for example in acute kidney injury (AKI).

Anuric and oliguric (<500ml/day) patients can be assumed to have a CrCl <10ml/min (severe renal impairment). Patients receiving renal replacement therapy with intermittent haemodialysis or peritoneal dialysis should be dosed the same as patients with a CrCl of less than 10ml/min unless otherwise stated.

Patients receiving continuous hemofiltration or haemodiafiltration are beyond the scope of this document.

Dosing regimens suggested reflect local practice for hospital inpatients and may be outside the scope of the product licence. Unlicensed doses are indicated in ***bold italics.*** The decision to prescribe an unlicensed dose should be considered along with the patient's clinical condition and infection being treated when choosing a dosing regimen. Patients should be closely monitored for signs of treatment efficacy and toxicity.

Antimicrobials that are removed by haemodialysis should be administered post dialysis where possible. This is particularly important where doses are administered once daily.

Bold italic text indicates that the dose is outside the product license.

	Creatinine Clearance (CrCl)	Dose recommended	Comments
Aciclovir IV	>50ml/min	Standard doses[1]	Monitor for neurotoxicity in renal impairment Eliminated by haemodialysis
	25-50ml/min	5-10mg/kg every 12 hours[1,2]	
	10-25ml/min	5-10mg/kg every 24 hours[1,2]	
	<10ml/min	***2.5-5mg/kg every 24 hours[2]***	
	Peritoneal dialysis or haemodialysis	2.5-5mg/kg every 24 hours[1,2]	

Amoxicillin IV/oral	>30 ml/min	Standard doses[1]	Higher doses may be required for treatment of endocarditis or meningitis - discuss with microbiology. Eliminated by haemodialysis
	≤30ml/min	***500mg - 1g every 8 hours[2]***	
Azithromycin IV/oral	>10ml/min	Standard doses[1]	Increased exposure in severe renal impairment – clinical significance unknown, use with caution[1,2] Unknown elimination by haemodialysis May be used in patients on tacrolimus who require treatment with a macrolide.
	<10ml/min	Standard doses[1,2]	
Benzylpenicillin IV	>20ml/min	***Standard doses[2]***	Dose depends on severity of infection. Monitor for neurotoxicity (e.g. seizures) at high doses. Eliminated by haemodialysis
	10-20ml/min	600mg – ***2.4g*** *every 6 hours[2]*	
	<10ml/min	600mg - ***1.2g*** *every 6 hours[2]*	
Cefalexin oral	>40ml/min	***Standard doses[2]***	Eliminated by haemodialysis
	10–40 ml/min	500mg every 8 hours[2,4]	
	<10ml/min	250mg every 8 hours[4] ***- 500mgevery 12 hours***[2]	
Ceftazidime IV	>50ml/min	Standard doses[1]	Higher doses have been used discuss with microbiology / pharmacy. Monitor for neurological side effects, consider checking levels. Eliminated by haemodialysis
	31-50ml/min	1 - ***2g*** every 12 hours[2]	
	16-30ml/min	1 - ***2g*** every 24 hours[2]	
	6-15ml/min Inc. APD/CAPD	500mg - ***1g*** every 24 hours[2]	
	<5ml/min	500mg - ***1g*** every 48 hours[2]	
	Haemodialysis (high flux)	1g every 48 hours or post dialysis[2]	
Ceftriaxone IV	>10ml/min	Standard doses[1,2]	Not eliminated by haemodialysis
	<10ml/min	Max 2g daily[1,2,4]	

Ciprofloxacin oral	>60ml/min	Standard doses[1]	Higher doses to be discussed with microbiology. Patients with renal impairment are at higher risk of tendon injury. Provide MHRA patient information leaflet about quinolone side effects. Unknown elimination by haemodialysis
	30-60ml/min	500mg every 12 hours[1]	
	10-30ml/min	500mg every ***12***-24hours[2]	
	<10ml/min	500mg every 24 hours[1] ***100% of normal dose may be used short term in exceptional circumstances[2]***	
Ciprofloxacin IV	>60ml/min	Standard doses[1]	Patients with renal impairment are at higher risk of tendon injury. Provide MHRA patient information leaflet about quinolone side effects. Unknown elimination by haemodialysis
	30-60ml/min	400mg every 12 hours[1]	
	10-30ml/min	400mg every ***12***-24 hours[2]	
	<10ml/min	400mg every 24 hours[1] ***100% of normal dose may be used short term in exceptional circumstances[2]***	
Clarithromycin IV/oral	>30ml/min	Standard doses[1]	Care! Check for significant interactions with transplant medication Unknown elimination by haemodialysis
	10-30ml/min	250mg-***500mg*** every 12 hours[2]	
	<10ml/min	250mg-***500mg*** every 12 hours[2]***High doses may cause vomiting.***	
Clindamycin oral	>10ml/min	Standard doses[1,2]	Care! Half-life is prolonged in severe renal impairment but clinical significance unknown. Monitor liver and renal function if treatment exceeds 10 days[4] Unknown elimination by haemodialysis
	<10ml/min	Standard doses[1,2]	
Clindamycin IV	>10ml/min	Standard doses[1]	
	<10ml/min	Standard doses [1,2]. Dosage may require reduction due to prolonged half-life[2].	
Co-amoxiclav oral	>30ml/min	Standard doses[1]	Care! With prolonged courses, clavulanic acid accumulates - monitor LFTs Eliminated by haemodialysis
	<30ml/min	***Standard doses[2]***	
Co-amoxiclav IV	>30ml/min	1.2 g every 8 hours[1]	
	<30ml/min	***1.2gevery 12 hours[2]***	

Co-trimoxazole IV/oral	>30ml/min	960mg every 12 hours[1]	Monitor FBC Higher doses required for treatment of PCP discuss with microbiology/ pharmacy. Serum creatinine may rise due to competition for renal secretion by trimethoprim. May cause hyperkalaemia. Eliminated by haemodialysis
	<30ml/min	***480mg every 12 hours*** [2]	
Doxycycline oral	All levels of renal function	Standard doses[1,2]	Unknown elimination by haemodialysis
Flucloxacillin oral	>10ml/min	Standard doses[1]	Monitor LFTs Not eliminated by haemodialysis
	<10ml/min	***Doses up to 1g every 6 hours[2]***	
Flucloxacillin IV	>10ml/min	Standard doses[1]	Consider levels if high doses required, monitor LFTs Not eliminated by haemodialysis
	<10ml/min	***Doses up to 1g every 6 hours[2]***	
Metronidazole IV/oral	All levels of renal function	Standard doses[1]	Eliminated by haemodialysis
Meropenem IV	>50ml/min	***500mgevery 6 hours***	Higher doses may be used – discuss with microbiology Eliminated by haemodialysis
	26-50ml/min	***500mgevery 8 hours***	
	10-25ml/min	500mg every 12 hours[1]	
	<10ml/min	500mg-1g every 24 hours[1,2]	
Nitrofurantoin oral	>30ml/min	Standard doses [1]	May be used with caution as short-course (3-7 days) therapy for treatment of uncomplicated lower UTI in CrCl 30-44ml/min when benefits expected to outweigh risks[1,4]
	≤30ml/min	Avoid[1,2,4]	
Penicillin V (phenoxymethylpenicillin) oral	All levels of renal function	***Standard doses[2]***	Eliminated by haemodialysis

Piperacillin/tazobactam IV	>20ml/min	4.5g every 8 hours[1]	Higher doses may be used in neutropenic sepsis or resistant infections - discuss with microbiology/ pharmacy. Eliminated by haemodialysis
	<20ml/min	4.5g every 12 hours[1]	
Pivmecillinam oral	All levels of renal function	Standard doses[1]	Unlikely to work if little residual renal function[2]. Accumulation may occur in severe renal impairment, use lower doses if using for extended periods of time[2]. Eliminated by haemodialysis Caution with long-term or frequently-repeated use due to possibility of carnitine depletion. Symptoms include muscle aches, fatigue, and confusion.
Rifampicin IV/oral	>10ml/min	Standard doses[2]	Check for significant interactions with transplant medication. Monitor LFTs. May colour PD fluid. Higher doses may be required for management of meningitis discuss with microbiology/ pharmacy. Not eliminated by haemodialysis
	<10ml/min	50-***100%*** of normal dose[2] (caution with doses >600mg[1])	
Trimethoprim oral	>30ml/min	Standard doses[1]	Serum creatinine may rise due to competition for renal secretion. May cause hyperkalaemia. Consider short term folic acid supplementation in CKD4-5[2] . Eliminated by haemodialysis
	15-30ml/min	***Standard doses[2]*** for short courses. Discuss with microbiology/ pharmacy if prolonged treatment doses required.	
	<15ml/min	50-***100%*** of dose[2]	

References

1. Individual manufacturers Summary of Product Characteristics. Available at: http://emc.medicines.org.uk/ Accessed 14th May 2021
2. The Renal Drug Database. The UK Renal Pharmacy Group. Available at: https://renaldrugdatabase.com/ Accessed 14th May 2021
3. British National Formulary. Available at: https://bnf.nice.org.uk/ Accessed 14th May 2021

Appendix C 4c COVID Mortality Score

Variable	4C Mortality Score
Age (years)	
<50	-
50-59	+2
60-69	+4
70-79	+6
≥80	+7
Sex at birth	
Female	-
Male	+1
No of comorbidities*	
0	-
1	+1
≥2	+2
Respiratory rate (breaths/min)	
<20	-
20-29	+1
≥30	+2
Peripheral oxygen saturation on room air (%)	
≥92	-
<92	+2
Glasgow coma scale score	
15	-
<15	+2
Urea (mmol/L)	
≤7	-
7-14	+1
>14	+3
C reactive protein (mg/dL)	
<50	-
50-99	+1
≥100	+2
*Comorbidities defined as chronic cardiac disease; chronic respiratory disease (excluding asthma); chronic renal disease (eGFR <30); mild to severe liver disease; dementia; diabetes mellitus (diet, tablet or insulin controlled); HIV/AIDS; malignancy; obesity.	

Appendix D NBT restricted antibiotic list

- Those antimicrobials listed below are restricted and must only be prescribed after discussion with an Infection Specialist or in line with the Trust Antimicrobial Guidelines.
- Prescribers must tick the “micro approved” box on the prescription chart and document in the medical notes when a discussion has taken place.
- Many of these antimicrobials are not held as ward stock and are available from pharmacy on a named patient basis only after confirmation that they have been approved by an Infection Specialist.
- Some restricted antimicrobials are held as ward stock to facilitate administration in specific indications detailed in the Trust Antimicrobial Guidelines. Use of these antimicrobials for indications outside of these guidelines requires prior approval by an Infection Specialist.
- Some restricted antimicrobials also require an electronic BlueTeq form to be completed prior to use – these are indicated below. Prior registration to the BlueTeq system is required – contact Pharmacy to facilitate this.

Agent	Additional info
Amikacin	
Amphotericin (IV)	
Anidulafungin	
Aztreonam	
Benzylpenicillin	
Caspofungin	
Cefazolin	
Cefiderocol	BlueTeq form required
Cefotaxime	
Ceftaroline	
Ceftazidime	
Ceftazidime / avibactam	BlueTeq form required
Ceftolozane / tazobactam	
Ceftriaxone	
Cefuroxime	
Chloramphenicol IV	
Ciprofloxacin IV	
Co-amoxiclav IV	
Colistin IV	
Dalbavancin	
Dapsone	
Daptomycin	
Ertapenem	
Erythromycin (IV and oral)	
Fidaxomicin	
Fluconazole IV	
Flucytosine	
Fosfomycin	
Gentamicin (nebulised)	
Isavuconazole	
Itraconazole	

Levofloxacin	
Linezolid	
Meropenem	
Micafungin	
Moxifloxacin	
Piperacillin / tazobactam	
Posaconazole	
Pristinamycin	
Remdesivir	BlueTeq form required
Rifampicin IV	
Rifaximin	
Streptomycin	
Temocillin	
Tigecycline	
Tobramycin (IV and nebulised)	
Voriconazole	