ANTIBIOTIC FORMULARY AND PRESCRIBING ADVICE FOR ADULT PATIENTS

VERSION 7.1
EFFECTIVE 16 DECEMBER 2016

THIS DOCUMENT SUPERSEDES ALL ANTIBIOTIC GUIDANCE FROM ANY SOURCE REGARDING ADULT PATIENTS DATED PRIOR TO THE ABOVE DATE

Northern Lincolnshire and Goole NHS Foundation Trust

United Lincolnshire Hospitals NHS Trust
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**Major Changes From Last Edition**

**Section 2**  Minor clarifications only

**Section 3**  3.1  Merged subsections into one table for ease of reference.

3.4.3.5  Clarifications around use of amikacin at NLaG/ULHT

**Section 4**  4.1.2  Minor clarifications only

4.1.3  Minor clarifications only

4.1.5  Minor clarifications only

4.3.2  Minor clarifications only

4.3.4  Clarified recommendations around duration of treatment

4.3.5  Changes to dosing regimens for Late onset/severe HAP

4.4.7  Minor clarification only

4.6  Amended subtitle to reflect content

4.6.1  Amended subtitle to clarify recommendations

4.6.3  Additional consideration added as per current practice

4.6.5  Changes to Meropenem dosing regimen for SBP

4.8.2  Clarifications around treating Sepsis when source identified

4.8.2  Clarifications around initial dose of antimicrobials in Severe Sepsis / Septic Shock

**Section 5**  5.4.6  Changes to prophylaxis in C-section

**Section 6**  Removed costing table

**Section 7**  Minor clarifications only

**Annexes**  Replaced old Annex 9 with Sepsis poster
1 Introduction

1.1 Aim

Antimicrobials and antibiotics are a very important part of the therapeutic regimen. They differ from all other drugs, however, in that the use of an antibiotic on one patient can affect many other patients through the selection of resistant organisms. To this end it is important that antibiotic use is controlled and profligate and unnecessary use, which selects for bacterial resistance, is avoided. The aim of this document is to encourage the appropriate use of this valuable resource.

Recent increases in the incidence of MRSA and *Clostridium difficile* infections have prompted a complete revision of the Antibiotic Policy. The recommendations made in this document are specifically targeted at reducing the risk of these organisms. As such, the use of cephalosporins and quinolones is heavily discouraged.

Specific instructions regarding difficult to treat organisms or infections are not included within the scope of this document, management of these organisms should be guided by reported sensitivities. National documents and references including the British National Formulary have been consulted.

1.2 Personnel

This document is aimed at all persons having prescribing rights for antibiotics, whether medically qualified or otherwise.

1.3 Areas Covered

This guidance applies to all areas served by the Northern Lincolnshire & Goole NHS Foundation Trust (NLAG) and United Lincolnshire Hospitals NHS Trust (ULHT).

1.4 Antimicrobials

Strictly speaking, antibiotics are compounds produced by micro-organisms to inhibit the growth of other micro-organisms. Chemically produced and modified compounds are not antibiotics and are more properly called antimicrobials. This difference is irrelevant in most clinical practice and thus the terms “Antibiotic” and “Antimicrobial” are used interchangeably throughout this document.

1.5 Samples

Appropriate antibiotic use is best achieved when the target organism is known. To this end appropriate samples require to be collected prior to the antibiotic being administered unless immediate empirical treatment is indicated. The procedures for collecting appropriate microbiological samples, whilst relevant, are beyond the scope of this document. Full details of these procedures can be found in the Path Links Laboratory Handbook on the intranet.

When culture and sensitivity test results become available, any prior antimicrobial prescription should be reviewed and amended as indicated to ensure prescription of the most appropriate antibiotics. Any amendment must be documented in the medical notes to show that culture and sensitivity results have been acted upon.

1.6 Contact Information

Advice regarding the appropriate use of antibiotics can be obtained from the Duty Consultant Microbiologist, contactable through switchboard.
2 Prescribing of Antimicrobials

This advice is intended to:

- Ensure all antimicrobial agents are **clinically indicated and essential**.
- Ensure any **allergy information** relating to antimicrobials is clearly recorded on the front of all the prescription charts, including the nature of the reaction.
- Ensure that prescriptions for antimicrobials are prescribed and administered at regular intervals.
- Ensure the **correct route** is prescribed.
- Ensure all antimicrobial prescriptions have a **specific indication documented** on the prescription chart AND in the medical records at the point of prescribing.
- Ensure all antimicrobial prescriptions have a "**review**" or "**stop**" date / length of course endorsed on the prescription chart at the point of prescribing. The duration should also be clear in the medical record.

- **Ensure all antimicrobials are reviewed at 48 hours** to focus therapy and either:
  - **Stop**
  - **De-escalate** from iv to oral therapy
  - **Change** to a narrow spectrum antibiotic
  - **Continue and review again** at 72 hours.

- Apply to all adult patients.
- Be used by medical, nursing and pharmacy staff.

2.1 General Points

Antimicrobials are only indicated when there is evidence of infection or when infection is to be actively avoided such as during surgery. The mere presence of an organism is not an indication for antimicrobials, thus an organism, even MRSA, isolated from a wound that is healing well with no signs of infection does not necessarily require antimicrobial treatment. Antimicrobials are not indicated for conditions that are generally of viral origin.

For serious or life-threatening infections (e.g. sepsis syndrome, meningitis, severe community acquired pneumonia) antibiotics should be prescribed and administered within one hour of presentation and, for less serious infections, within four hours.

All doses given in these guidelines, unless specifically indicated otherwise, assume broadly normal renal and hepatic function. Doses may need to be adjusted if renal and hepatic function is impaired.

If a course of antimicrobials has not led to a cure, it should not be automatically repeated. Instead, the diagnosis needs to be reviewed and specialist advice sought where necessary.

Please exercise additional caution in prescribing antimicrobials in elderly patients, those who have had previous *Clostridium difficile* disease, who are GDH-positive or those who are not being normally fed (especially TPN or NG/Peg feeding) because they are at increased risk of *C. difficile* disease.

2.2 Allergy Information (see Section 3.3 also)

Any allergies to antimicrobials need to be clearly documented in the medical notes and on the prescription chart.
2.3 Indication

The indication for all orders of antibiotics on the drug chart must be included on each order.

If there is not a specific box for this information on the prescription chart, the “Additional Instructions” or “Pharmacy” box must be used.

2.4 Timely Administration

The sooner patients with severe sepsis receive appropriate antibiotics the lower the mortality risk. All patients should receive appropriate antibiotics within 1 hour of severe sepsis onset. (Obtain blood cultures BEFORE administration of antibiotics where possible).

- The initial dose should be prescribed on the “once only” section of the prescription chart.
- The exact time of prescribing and administration should be clearly documented.
- The prescriber should inform the patient’s nurse of the need for urgent antibiotics
- Nurses should contact pharmacy as soon as possible if the required antibiotic is not stocked on the ward informing them of how urgent the antimicrobial is.

For more information please refer to the Sepsis Guidelines and Sepsis Care Bundle on the intranet.

It is good practice that the initial dose of any antimicrobial is prescribed on the “once only” section of the prescription chart, Care should be taken when prescribing the subsequent regular doses at the defined frequency to ensure this is taken in to account and avoid toxicity. Antimicrobials must be prescribed at a defined frequency, e.g. every 8 hours, to ensure antimicrobials are administered at regular intervals.

Thus dosing at 0600, 1400 and 2200 is acceptable but 0800, 1300, 1700 is NOT acceptable. Whilst there is an understandable tendency to adjust dosing times to fit with nursing medication rounds where possible, this should not be permitted to interfere with the above.

2.5 Course Duration and “Stop”/“Review” Date

All prescribers must document the intended duration on the prescription chart for all orders of antimicrobial agents. A “stop” / “review” date must be clearly indicated on the prescription chart at the point of prescribing any antimicrobial agent.

If there is not a specific box for any information on the prescription chart, the “Additional instructions” or “Pharmacy” box may be used.

2.5.1 Oral Antimicrobial Therapy

The average length of an oral course is assumed to be 5 days unless otherwise stated in the guidelines.

For some patients it may be difficult to endorse a definite stop date until the patient’s condition begins to improve. Antimicrobial agents in these cases should have a review date about twice a week (e.g. Consultant ward rounds and/or Fridays). As a minimum, oral prescriptions should be reviewed after 5 days and any reason for continuation must be documented in medical notes.
2.5.2 IV Antimicrobial Therapy

In patients with a severe infection who initially require iv antimicrobial therapy, they can be switched to oral therapy within 48 hours in the majority of cases with a number of advantages:

- Reduction in the likelihood of hospital acquired iv access associated infection.
- Reduce patient discomfort, improve mobility and possibly increase the potential for earlier hospital discharge.
- Save both medical and nursing time.
- Potentially reduce treatment costs.
- Potentially reduce the risk of adverse incidences; errors in preparation are significantly higher with parenteral drugs, compared with oral formulations.

The majority of iv antimicrobial agents will therefore require a “review” rather than a “stop” date prior to being converted to oral.

For any intravenous antimicrobials that are continued beyond 48 hours duration, the reason for continuation must be documented in the medical notes.

Intravenous antimicrobials that are re-prescribed beyond 48 hours should be reviewed daily. The decision on continuation/completion of antimicrobial therapy must be documented in the medical notes.

2.5.3 Review of Antimicrobial Therapy

There is the need to embed a “Start Smart – Then Focus” prescribing culture with daily review and documented evidence of an active review of all antibiotics after 48 hours. A day 3 prescribing decision should be documented within the notes, focusing therapy in line with cultures / sensitivities / additional clinical information on the patient at 48 hours to either:

- Stop
- De-escalate from iv to oral therapy
- Change to a narrow spectrum antibiotic
- Continue and review again at 72 hours

2.5.3.1 IV To Oral Switch Criteria

Suitability for the early switch from iv to oral therapy should be assessed by the attending clinician on a case-by-case basis but patients should generally have all of the “COMS” criteria.

“COMS” criteria to consider:

- Clinical improvement observed
- Oral route is not compromised and suitable oral antimicrobial option is available (see Section 6 for recommended oral switches and costs). N.B. If NG / PEG feeding then please consult your ward Pharmacist.
- Markers indicate a trend towards normal
- Specific indication / deep-seated infection not present (see exceptions*)

*Exceptions:
• Deep-seated infections (may require an initial 2 weeks of iv therapy but seek microbiology advice)
  - Osteomyelitis, septic arthritis (N.B. high-dose oral clindamycin may be appropriate once patient is stable – seek microbiology advice).

• High risk infections requiring prolonged iv therapy (seek microbiology advice regarding the length of treatment):
  - Endocarditis
  - Exacerbations of cystic fibrosis/bronchiectasis
  - Infected implants/prosthetics
  - Intracranial abscesses
  - Legionella pneumonia
  - Mediastinitis
  - Meningitis/encephalitis
  - Severe infections during chemotherapy-related neutropenia
  - Severe or necrotising soft tissue infections
  - *Staphylococcus aureus or Pseudomonas spp*bacteraemia

• Certain multi-resistant organisms may require treatment with agents that are only available in an iv form (seek microbiology advice regarding length of treatment).

For a specific indication / deep-seated infection it is still appropriate to prescribe a review date to ensure clinical response. Antimicrobial agents in these cases should have a review date at least once a week (e.g. Consultant ward rounds and/or Fridays). It is recommended that longer term iv prescriptions should be reviewed after 5 days.

2.5.3.2 Recording the Route of Administration

When a course of antimicrobials is initiated, or switched from IV to oral, the route of administration must not only be entered onto the prescription chart, but must also be recorded in the medical notes.

2.6 Actions for Healthcare Professionals

2.6.1 Actions For Doctors

• Prior to prescribing any antibiotic **confirm the allergy status** of a patient, including the nature of the reaction. Ensure that the allergy box on the front of the prescription chart is completed.

• All prescriptions for antimicrobials should include an indication (enter in the Pharmacy/ ‘Additional Instructions’ box).

• **Write a “stop” date / intended course duration or a “review” date on the prescription chart for each antimicrobial agent prescribed.**

• The majority of iv antimicrobial therapy will require a “review” date rather than a “stop” date prior to being converted to oral. (See exceptions*)

• Review points should be targeted for lunchtime doses where possible and should avoid weekends unless the patient is due for daily Consultant review.

• Antimicrobial review should be clearly documented in the medical notes AND on the chart by completing and signing the review box where available. If there is not a review box, the ‘Additional Instructions’ or ‘Pharmacy’ box may be used. Endorse a new review date if to continue.

  - For some infections it may be difficult to endorse a definite review / stop date until the patient’s clinical condition begins to improve. Antimicrobials in these circumstances
should have review dates about twice a week (e.g. Consultant ward rounds and/or Fridays).

- Following an iv to oral switch a stop / course duration must be endorsed for each as either of the following:
  - “….. days more” i.e. …days of oral following iv therapy
  - “….. days in total” i.e. the total required duration of iv and po together
  - Or put a stop date (e.g. “stop 09/08/2010”)

- Antimicrobial agents should be stopped / reviewed earlier than the date shown if clinically indicated.

Example with stop date (mostly appropriate for oral therapy):

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<th>03/08</th>
<th>04/08</th>
<th>05/08</th>
<th>06/08</th>
<th>07/08</th>
<th>08/08</th>
<th>09/08</th>
</tr>
</thead>
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<tr>
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<td>Nitrofurantoin</td>
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<td></td>
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</tr>
<tr>
<td>Dose</td>
<td>50mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Route</td>
<td>PO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start Date</td>
<td>03/08/10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td>A Doctor</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bleep or Ext.</td>
<td>12</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pharmacy / Additional instructions</td>
<td>3 days for UTI</td>
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<td></td>
</tr>
</tbody>
</table>

Example with review date (mostly appropriate for initial IV therapy):

<table>
<thead>
<tr>
<th>Date:</th>
<th>03/08</th>
<th>04/08</th>
<th>05/08</th>
<th>06/08</th>
<th>07/08</th>
<th>08/08</th>
<th>09/08</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Name</td>
<td>Flucloxacillin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>1g</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Route</td>
<td>IV</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start Date</td>
<td>03/08/10</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td>A Doctor</td>
<td></td>
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</tr>
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<tr>
<td>Additional Instructions</td>
<td>Cellulitis Review route 48 hours</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

NOTE:

When rewriting treatment sheets containing prescriptions for antibiotics, ensure that the ORIGINAL START DATE of any antibiotic prescription which needs to be continued is transferred onto the new prescription for that antibiotic, rather than the date the treatment sheet is rewritten.
2.6.2 Actions For Nurses

- Prior to administering any antibiotic confirm the allergy status of a patient, including the nature of the reaction. Ensure that the allergy box on the front of the prescription chart is completed by a prescriber or appropriate member of pharmacy.

- Request the Dr to write a “review” / “stop” date on the prescription chart for all antimicrobial agents where appropriate (see exceptions*).

- Query all prescriptions continuing beyond the “review” / “stop” dates without a review being apparent.

- Whilst awaiting review continue to administer the antimicrobial

- Ask the Dr to review a prescription if a number of doses have been missed during the prescribed course, especially if the patient is still unwell or at a weekend where regular review is unlikely.

2.6.3 Actions For Pharmacists

- Prior to checking and/or supplying any antibiotic confirm the allergy status of a patient, including the nature of the reaction. Ensure that the allergy box on the front of the prescription chart is completed.

- Ensure all prescriptions for restricted antibiotics adhere to the Antibiotic Formulary and Prescribing Advice.

- Request an indication and “review” / “stop” date to be written on the prescription chart for all antimicrobial agents

- Inform the prescriber that the standard is to include a specific indication and “review” / “stop” date every time an order for an antimicrobial agent is made (see exceptions*). This request should be made within 48-72 hours of the prescription being written.

- If the prescription is written in the presence of a Pharmacist, request an indication and “review” / “stop” date as part of the prescription writing process.

- Query all prescriptions continuing beyond the “review” / “stop” dates without a review being apparent.

- Ask the doctor to review a prescription if a number of doses have been missed during the prescribed course, especially if the patient is still unwell or at a weekend where regular review is unlikely.

If the above is not possible, write in the notes requesting for a “review” / “stop” date for the antimicrobial agent or annotate the prescription chart “review route”. Review of dosage points should be targeted for lunchtime doses where possible and should avoid weekends unless the patient is due for daily Consultant review.

2.7 De-escalation Of IV To Oral

Please see Section 6.
3 Notes on Specific Compounds

3.1 List of Antimicrobials

Freely available agents do not require Consultant Microbiologist approval.

All other agents will require the name of the Microbiologist consulted to be endorsed on the prescription unless prescribed for a permitted indication as per the table below.

<table>
<thead>
<tr>
<th>Agent (and route)</th>
<th>Permitted Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir (iv/po)</td>
<td>Freely available</td>
</tr>
<tr>
<td>Amikacin (im/iv)</td>
<td>Intravitreal use permitted for endophthalmitis, as per guidelines Microbiologist approval required for iv treatment</td>
</tr>
<tr>
<td>Amoxicillin (iv/po)</td>
<td>Freely available</td>
</tr>
<tr>
<td>Ampicillin (iv)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Anidulafungin (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Anti-mycobacterial Agents</td>
<td>TB. Consultant Respiratory Physician input advised</td>
</tr>
<tr>
<td>Azithromycin (po)</td>
<td>Antibody deficiency syndromes Bronchiectasis Sexual Health use (chlamydia, gonorrhoea) Surgical prophylaxis in Obs &amp; Gynae as per guidelines</td>
</tr>
<tr>
<td>Azithromycin (iv)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Aztreonam (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Benzylpenicillin (iv)</td>
<td>Freely available</td>
</tr>
<tr>
<td>Cefaclor (po)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Cefadroxil (po)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Cefalexin (po)</td>
<td>Urinary Tract Infection (500mg oral doses 8 hourly, when switching from IV cefuroxime, patient pregnant, or other situations where none of the other oral agents are suitable)</td>
</tr>
<tr>
<td>Cefixime (po)</td>
<td>Sexual Health use only. For 400mg oral stat dose in pelvic inflammatory disease where intramuscular injection is contraindicated or refused by patient.</td>
</tr>
<tr>
<td>Cefotaxime (iv)</td>
<td>Epiglottitis (1st line) Meningitis of unknown aetiology or haemophilus origin (1st line) Pneumococcal/ meningococcal meningitis (2nd line, if minor penicillin rash)</td>
</tr>
<tr>
<td>Cefpodoxime (po)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Cefradine (iv/po)</td>
<td>Not on formulary and NOT stocked</td>
</tr>
<tr>
<td>Ceftaroline (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>Intravitreal use permitted for endophthalmitis, as per guidelines IV use permitted in Cystic Fibrosis, and for Oncology/Haematology</td>
</tr>
<tr>
<td>Ceftobiprole (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Ceftriaxone (im/iv)</td>
<td>Epididymo-orchitis - part of 1st line regiment for patients &lt; 35yrs old. Meningitis - an alternative to 1st / 2nd line cefotaxime, once diagnosis is confirmed. Pelvic Inflammatory Disease – im or iv stat dose, as per guidelines</td>
</tr>
<tr>
<td>Agent (and route)</td>
<td>Permitted Indications</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------</td>
</tr>
</tbody>
</table>
| **Cefuroxime (iv)** | Second line agent where minor penicillin rash:  
- Aspiration pneumonia  
- CAP CURB65 ≥3  
- Cellulitis as per flow chart  
- Chorio-amnionitis  
- Early onset HAP of moderate severity (as opposed to mild)  
- Facial cellulitis  
- Open fracture  
- Pelvic Inflammatory Disease, post op or where STI not suspected  
- Periorbital cellulitis  
- Peritonitis  
- Puerperal sepsis, or septic abortion  
- Sepsis of unknown origin  
- Surgical prophylaxis as per guidelines  
| Part of first line prophylaxis for caesarean section (if prophylaxis being administered pre-cord clamping) |
| **Cefuroxime axetil (po)** | Not on formulary and NOT stocked |
| **Chloramphenicol (iv/po)** | Microbiologist approval required in all cases |
| **Chloramphenicol (topical)** | Freely available |
| **Ciprofloxacin (iv/po)** | IV use is only permitted without authorisation code where ciprofloxacin use is indicated (as below) and the patient is unable to take ANY oral medication |
| **Penicillin allergy:** |  
- Cholecystitis  
- GI bleed secondary to hepatic cirrhosis  
- Hepatic abscess  
- Hepato-biliary sepsis  
- Neutropenic sepsis (as part of 3rd line treatment regimen)  
- Non-lactational breast abscess  
- Peri orbital cellulitis (2nd or 3rd line, depending on setting)  
- Peritonitis (instead of gentamicin if nephrotoxicity / AKI concerns)  
- Pyelonephritis  
- Sepsis of unknown origin (3rd line)  
- Severe (grade 4) diabetic foot infection (with or without MRSA)  
- Severe Bites (may use iv initially)  
| As part of Local Cancer Unit protocols  
Cellulitis associated with fresh water immersion  
Chronic Prostatitis (2nd line)  
Discitis  
Epididymo-orchitis (where STI not suspected)  
Malignant **otitis externa**  
Prostate biopsy  
<p>| <strong>Clarithromycin (iv/po)</strong> | Freely available |</p>
<table>
<thead>
<tr>
<th>Agent (and route)</th>
<th>Permitted Indications</th>
</tr>
</thead>
</table>
| **Clindamycin (iv/po)** | Necrotising fasciitis (as part of 1st line treatment regimen)  
| Penicillin allergy: | - Cellulitis (facial, orbital and periorbital)  
| | - Chorio-amnionitis (Group B Strep)  
| | - Diabetic foot  
| | - Erysipelas  
| | - Pelvic inflammatory disease  
| | - Pelvic inflammatory disease (part of 2nd line regimen if pregnant)  
| | - Sepsis syndrome (3rd line)  
| | - Septic arthritis  
| | - Severe bites (as part of 2nd line regimen)  
| | - Surgical site infections  
| | - Prevention of neonatal sepsis with Group B strep  
| | Prophylaxis in:  
| | caesarean section  
| | facial surgery  
| | perineal tear  
| | removal of placenta  
| | total abdominal hysterectomy  
| | vaginal approach surgery  
| | vaginal hysterectomy, anterior / posterior repair |
| **Co-amoxiclav (iv/po)** | Freely available |
| **Co-fluampicil [Magnapen]** | Not on the formulary and NOT stocked |
| **Colistin (iv)** | Microbiologist approval required in all cases |
| **Colistin (nebulised)** | Respiratory Physician use only (reserved for Gram-negative infections resistant to first-line agents) |
| **Cotrimoxazole (iv/po)** | Pneumocystis prophylaxis and treatment  
| Penicillin allergy: | - Meningitis of unknown aetiology if age > 55 or immunocompromised  
| | - Listeria meningitis |
| **Daptomycin (iv)** | Microbiologist approval required in all cases |
| **Doxycycline (po)** | Freely available |
| **Ertapenem (po)** | Microbiologist approval required in all cases |
| **Erythromycin (iv/po)** | Breast abscess (if penicillin allergy and breast feeding)  
| | Pregnancy, where macrolide required  
| | Prokinetic agent in Critical care  
| | Sexual Health (specialist use only) |
| **Fidaxomicin (po)** | Microbiologist approval required in all cases |
| **Flucloxacillin (iv/po)** | Freely available |
| **Fosfomycin (iv/po)** | Microbiologist approval required in all cases |
| **Fusidic Acid (iv/po)** | Microbiologist approval required in all cases |
| **Fusidic Acid (topical)** | Freely available |
| **Gentamicin (im/iv)** | Freely available |
| **Imipenem/cilastatin (iv)** | Microbiologist approval required in all cases |
| **Isavuconazole (iv/po)** | Microbiologist approval required in all cases |
| **Levofoxacin (iv/po)** | Microbiologist approval required in all cases |
| **Linezolid (iv/po)** | Microbiologist approval required in all cases |

**BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS**
BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS

<table>
<thead>
<tr>
<th>Agent (and route)</th>
<th>Permitted Indications</th>
</tr>
</thead>
</table>
| Meropenem (iv)    | Brain abscess (part of 1st line regimen)*  
                   | Infective endocarditis (native valve where there is risk factor for presence of multi-resistant Gram-negative organisms)*  
                   | Late onset hospital acquired pneumonia (if minor penicillin rash)  
                   | Necrotising fasciitis (part of 1st line regimen)*  
                   | Neutropenic sepsis (if minor penicillin rash)  
                   | Orbital (post-septal) cellulitis (1st line)*  
                   | Prostate biopsy (if multi-resistant organism previously isolated)*  
                   | Spontaneous bacterial peritonitis (1st line)*  
                   | *These indications still require urgent discussion with a Consultant Microbiologist |
| Methenamine       | Not on the formulary and NOT stocked |
| Metronidazole (iv/po/pr) | Freely available |
| Moxifloxacin (iv/po) | Microbiologist approval required in all cases |
| Nalidixic Acid    | Not on the formulary and NOT stocked |
| Neomycin (po)     | Gut sterilisation/Colonic bacterial load reduction in hepatic failure |
| Netilmicin        | Not on the formulary and NOT stocked |
| Nitrofurantooin (po) | Freely available |
| Norfloxacin       | Not on the formulary and NOT stocked |
| Ofloxacin (po)    | Ophthalmology (rarely)  
                   | Pelvic inflammatory disease (in penicillin allergy where 2nd line regimen not suitable)  
                   | Sexual Health use  
                   | Urology (BCG bladder instillation) |
| Ofloxacin (topical) | Ophthalmology use only |
| Oxytetracycline (po) | Dermatology use only |
| Phenoxymerpenicillin (po) (also known as Penicillin V) | Freely available |
| Piperacillin/tazobactam [Tazocin](iv) | Acute prostatitis (part of 1st line regimen)  
                   | Cholecystitis (1st line)  
                   | Confirmed Pseudomonas Infection / Sepsis  
                   | GI bleed secondary to hepatic cirrhosis (1st line)  
                   | Hepato-biliary sepsis  
                   | Malignant otitis externa (1st line)  
                   | Neutropenic sepsis (part of 1st line regimen)  
                   | Periorbital cellulitis (1st line)  
                   | Sepsis of unknown origin (part of 1st line regimen)  
                   | Severe / Late onset hospital acquired pneumonia (1st line)  
                   | Severe diabetic foot (Grade 4) (1st line) |
| Pivmecillinam (po) | Resistant urinary tract Infections where no other oral agent is suitable |
| Rifampicin (iv/po) | Brain abscesses(as part of 1st line regimen)  
                   | Discitis (part of 1st line regimen)  
                   | Infective endocarditis (prosthetic valve/ intracardiac prosthesis)  
                   | Meningitis (pneumococcal)  
<pre><code>               | Tuberculosis – must have input of chest physician |
</code></pre>
<p>| Rifaximin (po)    | For initiation by Consultant Gastroenterologist for hepatic encephalopathy prophylaxis only. |
| Spectinomycin     | Sexual Health use only |</p>
<table>
<thead>
<tr>
<th>Agent (and route)</th>
<th>Permitted Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin (iv)</td>
<td>Microbiologist approval required in all cases except in TB</td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td>Tedizolid (iv/po)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td></td>
<td>Uncomplicated insertion of cardiac pacemaker or similar device (1st line)</td>
</tr>
<tr>
<td></td>
<td>Vascular Surgery – Insertion Of Graft Or Patch / Vein Graft Reversal (1st line)</td>
</tr>
<tr>
<td></td>
<td>Penicillin allergy:</td>
</tr>
<tr>
<td></td>
<td>- Endocarditis prophylaxis</td>
</tr>
<tr>
<td></td>
<td>- Open fracture</td>
</tr>
<tr>
<td></td>
<td>- Surgical prophylaxis</td>
</tr>
<tr>
<td></td>
<td>Arthroplasty</td>
</tr>
<tr>
<td></td>
<td>Breast surgery</td>
</tr>
<tr>
<td></td>
<td>Elective procedures on soft tissue of the hand</td>
</tr>
<tr>
<td></td>
<td>Elective Splenectomy</td>
</tr>
<tr>
<td></td>
<td>Flap Surgery For Pilonidal Sinus</td>
</tr>
<tr>
<td></td>
<td>Head and Neck surgery</td>
</tr>
<tr>
<td></td>
<td>Hip fracture – DHS</td>
</tr>
<tr>
<td></td>
<td>Open surgery for closed fracture</td>
</tr>
<tr>
<td></td>
<td>Spinal surgery</td>
</tr>
<tr>
<td></td>
<td>Vascular surgery – Amputation</td>
</tr>
<tr>
<td>Teicoplanin (im/iv)</td>
<td></td>
</tr>
<tr>
<td>Telithromycin</td>
<td>Not on the formulary and NOT stocked</td>
</tr>
<tr>
<td>Temocillin (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Ticarcillin [Timentin]</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td></td>
<td>Only made available during piperacillin/tazobactam shortage</td>
</tr>
<tr>
<td>Tigecycline (iv)</td>
<td>Microbiologist approval required in all cases</td>
</tr>
<tr>
<td>Tobramycin (iv)</td>
<td>Pseudomonas disease especially respiratory</td>
</tr>
<tr>
<td>Tobramycin (nebulised)</td>
<td>Respiratory Physician use only</td>
</tr>
<tr>
<td>Trimethoprim (po)</td>
<td>Freely available</td>
</tr>
<tr>
<td>Vancomycin (iv)</td>
<td>Freely available</td>
</tr>
<tr>
<td>Vancomycin (po)</td>
<td>Severe Clostridium difficile infection only</td>
</tr>
</tbody>
</table>
3.2 Note On The Use of Co-amoxiclav

It has become obvious over recent years that there are times when the standard doses of co-amoxiclav are inadequate. Increasing the clavulanic acid component beyond 0.8 g/day is NOT recommended. However, the amoxicillin component can safely be increased as far as 12 g/day. The table below illustrates how to prescribe increasing doses of co-amoxiclav.

**Dose Ladder For Co-amoxiclav**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>375mg co-amoxiclav</td>
<td>Oral</td>
<td>Every 8 hours</td>
<td>Dose is below recommended dose - if liquid formulation required prescribe co-amoxiclav 375mg dispersible tablets (250mg amoxicillin equivalent)</td>
</tr>
<tr>
<td>625mg co-amoxiclav</td>
<td>Oral</td>
<td>Every 8 hours</td>
<td>Normal oral dose - if liquid formulation required prescribe 10ml co-amoxiclav 250/62.5 suspension (500mg amoxicillin equivalent)</td>
</tr>
<tr>
<td>750mg co-amoxiclav</td>
<td>Oral</td>
<td>Every 8 hours</td>
<td>Avoid if possible – use 625mg instead</td>
</tr>
<tr>
<td>625mg co-amoxiclav</td>
<td>Oral</td>
<td>Every 8 hours</td>
<td>Maximum oral dose (1g amoxicillin equivalent) Prescribe co-amoxiclav 625mg plus amoxicillin 500mg.</td>
</tr>
<tr>
<td>600mg co-amoxiclav</td>
<td>Intravenous</td>
<td>Every 8 hours</td>
<td>Dose is below recommended dose and usually reserved for use in renal impairment – consider 1.2g instead.</td>
</tr>
<tr>
<td>1.2g co-amoxiclav</td>
<td>Intravenous</td>
<td>Every 8 hours</td>
<td>Normal parenteral dose (3g amoxicillin/day equivalent)</td>
</tr>
</tbody>
</table>

**When Increased Doses Are Required**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2g co-amoxiclav</td>
<td>Intravenous</td>
<td>Every 6 hours</td>
<td>MAXIMUM daily dose of clavulanate (4g amoxicillin/day equivalent)</td>
</tr>
<tr>
<td>1.2g co-amoxiclav</td>
<td>Intravenous</td>
<td>Every 8 hours</td>
<td>(6g amoxicillin/day equivalent)</td>
</tr>
<tr>
<td>PLUS 1g amoxicillin</td>
<td>Intravenous</td>
<td>Every 6 hours</td>
<td>(8g amoxicillin/day equivalent)</td>
</tr>
<tr>
<td>PLUS 2g amoxicillin</td>
<td>Intravenous</td>
<td>Every 8 hours</td>
<td>(9g amoxicillin/day equivalent)</td>
</tr>
<tr>
<td>PLUS 2g amoxicillin</td>
<td>Intravenous</td>
<td>Every 6 hours</td>
<td>(12g amoxicillin/day equivalent)</td>
</tr>
</tbody>
</table>

3.3 Note On Penicillin Allergy

“Penicillin allergy” appears to be very common in hospitalised patients, being listed in the known drug allergies in up to half of in-patients. In practice genuine penicillin allergy is significantly rarer.
Before any patient is labelled penicillin allergic, confirm that the allergy is genuine.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting, abdominal pain:</td>
<td>Frequently accompany oral antibiotics use. These are not usually allergies.</td>
</tr>
<tr>
<td>Maculopapular rash developing several days into a course of antibiotics</td>
<td>May be a non-allergic rash, particularly common with amoxicillin given during EBV infection. Any features of Stevens-Johnson syndrome should result in immediate discontinuation of the drug and prohibition of use in the future.</td>
</tr>
<tr>
<td>Immediate onset angioedema, rhinitis, dyspnoea, wheeze, hypotension, etc</td>
<td>These are very suspicious of IgE mediated allergy. Do not use any beta-lactam if a beta-lactam was the provoking drug. Do NOT use a “test dose” to “find out”. Discuss cefalosporin or carbapenem use with Consultant Microbiologist.</td>
</tr>
<tr>
<td>“My mum told me I was allergic to penicillin, I don’t know why”</td>
<td>Each case will need individual assessment. A specific IgE blood test for IgE against penicillin compounds is specific, but very insensitive. A negative penicillin “RAST” test therefore by no means excludes penicillin allergy.</td>
</tr>
</tbody>
</table>

Please note:

- Penicillin allergy is NOT inherited. Testing is NOT indicated even if a relative has true penicillin allergy.
- Skin testing for penicillin is the ‘gold standard’ but reagents for this have stopped being manufactured and this service cannot be offered by the Immunology Department at the present time.
- A detailed history including timing and type of reaction is essential in assessing patients with possible drug allergy.

It is often valuable to check previous drug administration sheets to determine whether or not the patient has received a penicillin in the past without adverse effect.

List of Penicillin-containing antibiotics

- Benzylpenicillin
- Phenoxymethylpenicillin
- Flucloxacillin
- Amoxicillin
- Co-Amoxiclav (Augmentin)
- Co-fluampicil (Magnapen)
- Temocillin
- Piperacillin
- Piperacillin/tazobactam (Tazocin)
- Ticarcillin
- Ticarcillin/clavulanate (Timentin)
List of Other Beta-lactam Antibiotics

Patients with a penicillin allergy (history of anaphylaxis, urticaria, Stevens-Johnson syndrome, or rash immediately after penicillin administration) SHOULD NOT receive a penicillin or any other beta-lactam antibiotic listed below.

If a patient has a minor rash (ie non confluent, non-pruritic rash restricted to a small area of the body), with a penicillin or a rash that appears more than 72 hours after administration, they may be able to safely tolerate another beta-lactam antibiotic such as those below but proceed with caution.

Please seek expert microbiology advice in cases of SEVERE infections.

<table>
<thead>
<tr>
<th>Aztreonam</th>
<th>Cefuroxime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefalexin</td>
<td>Cefradroxil</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>Cefixime</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Ceftazidime</td>
</tr>
<tr>
<td>Pivmecillinam</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>Cefaroline</td>
<td></td>
</tr>
</tbody>
</table>


3.3.1 Inadvertent administration of a beta-lactam based antibiotic to a patient with a history of adverse reactions to penicillin, with no apparent reaction.

Administration of a penicillin based antibiotic to a patient with a previously recorded adverse reaction is a serious clinical error, and all efforts to avoid it must be made. However, it is acknowledged that this error does occasionally occur, and the result can yield useful information which may be of benefit to the patient.

First there must be duty of candour – discuss the situation with the patient and apologise for the error. Involve the Consultant in charge of the patient’s care as soon as practical. Complete an incident report form (IR1).

<table>
<thead>
<tr>
<th>Nature of previous reaction</th>
<th>Mechanism</th>
<th>Action to be taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis, angioedema, acute urticaria</td>
<td>Type 1 hypersensitivity</td>
<td>Inadvertent test of hypersensitivity. If no reaction at first dose, risk of reaction to subsequent doses is no greater than for the rest of the population. Reassure patient and re-label notes as not Type 1 hypersensitivity.</td>
</tr>
<tr>
<td>Stevens-Johnson syndrome, erythema multiforme, severe mouth ulcers, toxic epidermal necrolysis (TEN)</td>
<td>Delayed hypersensitivity, drug acts as a hapten</td>
<td>Stop the antibiotic immediately and discuss with a Microbiologist. Careful history regarding timing of antibiotics in previous reaction needed – it may have been the underlying infection that caused the reaction.</td>
</tr>
<tr>
<td>Rash after amoxicillin for sore throat</td>
<td>Amoxicillin / EBV effect</td>
<td>Reassure. If symptoms recur, reclassify as delayed onset rash.</td>
</tr>
<tr>
<td>Delayed onset rash</td>
<td>T-cell mediated</td>
<td>If single dose only, switch to an alternative agent. If 2 or more doses, watch and manage symptoms if they occur. If no reaction, reassure and re-label.</td>
</tr>
<tr>
<td>Drug fever / serum sickness-like reaction</td>
<td>Immune complex / type III</td>
<td>Review need for antibiotics. Discuss alternatives with a Microbiologist</td>
</tr>
<tr>
<td>Nausea, vomiting or diarrhoea</td>
<td>GI intolerance</td>
<td>Reassure patient. If symptoms recur, review need for antibiotics. Discuss alternatives with a Microbiologist if necessary.</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> colitis or previous GDH positivity</td>
<td>Imbalance of GI flora</td>
<td>Review need for antibiotics. Discuss alternatives with a Microbiologist</td>
</tr>
<tr>
<td>Thrush</td>
<td>Super-infection with <em>Candida</em> spp.</td>
<td>Should resolve on stopping antibiotics. Manage symptoms according to the antibiotic formulary.</td>
</tr>
<tr>
<td>HIV disease-related drug reaction</td>
<td>CD4 &lt;200</td>
<td>Seek specialist advice.</td>
</tr>
<tr>
<td>Unknown</td>
<td>Unknown</td>
<td>If no reaction, continue antibiotic and watch for symptoms. If they occur, manage accordingly. If not, reassure and re-label.</td>
</tr>
</tbody>
</table>

If the patient is found not to be allergic to the agent administered, communicate the finding to the rest of the medical and nursing team, re-label the medical records and drug chart, explain to and reassure the patient, and inform the GP.
3.4 Therapeutic Drug Monitoring

Antibiotic Assays

Vancomycin, gentamicin and tobramycin assays are performed by Path Links Blood Sciences.

There is a limited capacity for Therapeutic Drug Monitoring (TDM) of antibiotics other than gentamicin, tobramycin and vancomycin.

Amikacin levels may be monitored by prior arrangement with the Consultant Microbiologist.

The need for testing levels of other drugs must be discussed with the Consultant Microbiologist prior to sending any samples.

3.4.1 Creatinine Clearance (Cockcroft-Gault)

In many cases, the eGFR as displayed on WebV is not adequate for the calculation of creatinine clearance for TDM purposes. The Cockcroft-Gault Creatinine Clearance estimates using the different formulas listed in the sections below must be used instead.

3.4.2 Glycopeptides

3.4.2.1 Vancomycin

Vancomycin is used intravenously to treat serious gram-positive infections, including those caused by methicillin-resistant *Staphylococcus aureus* (MRSA).

Currently, the recommended target pre-dose (‘trough’) concentration should be in the range 10-15mg/L for standard infection and 15-20mg/L for MRSA and deep seated infections (e.g. osteomyelitis, endocarditis and pneumonia due to *Staphylococcus aureus*). Monitoring of peak levels is not required.

**Vancomycin Loading Dose** (Based on actual body weight, independent of renal function/age)

<table>
<thead>
<tr>
<th>Actual body weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.  &lt; 40 kg</td>
<td>750mg in 250ml sodium chloride 0.9% over 1.5 hours</td>
</tr>
<tr>
<td>2.  40 - 59 kg</td>
<td>1g in 250ml sodium chloride 0.9% over 2 hours</td>
</tr>
<tr>
<td>3.  60 – 90 kg</td>
<td>1.5g in 500ml sodium chloride 0.9% over 2.5 hours</td>
</tr>
<tr>
<td>4.  &gt; 90 kg</td>
<td>2g in 500ml sodium chloride 0.9% over 3.5 hours</td>
</tr>
</tbody>
</table>

Calculate creatinine clearance (mL/minute):-

Men: \[1.23 \times (140 – \text{age}) \times \text{Actual Body Weight* in kg} \]
\[\text{Serum creatinine (micromol/L)}\]

Women: \[1.04 \times (140 – \text{age}) \times \text{Actual Body Weight* in kg} \]
\[\text{Serum creatinine (micromol/L)}\]

*The table below should be used to determine whether patients are classified as obese (>20% over ideal body weight) and to determine, if they are, the maximum body weight for use in the Cockcroft-Gault equation above.
Maximum Body Weight Table

<table>
<thead>
<tr>
<th>Height (ft inches)</th>
<th>Height (cm)</th>
<th>MBW (kg) Male</th>
<th>MBW (kg) Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>4' 8&quot;</td>
<td>142</td>
<td>49</td>
<td>43</td>
</tr>
<tr>
<td>4' 9&quot;</td>
<td>145</td>
<td>52</td>
<td>47</td>
</tr>
<tr>
<td>4' 10&quot;</td>
<td>147</td>
<td>54</td>
<td>49</td>
</tr>
<tr>
<td>4' 11&quot;</td>
<td>150</td>
<td>58</td>
<td>52</td>
</tr>
<tr>
<td>5' 0&quot;</td>
<td>152</td>
<td>60</td>
<td>55</td>
</tr>
<tr>
<td>5' 1&quot;</td>
<td>155</td>
<td>62</td>
<td>58</td>
</tr>
<tr>
<td>5' 2&quot;</td>
<td>158</td>
<td>66</td>
<td>60</td>
</tr>
<tr>
<td>5' 3&quot;</td>
<td>160</td>
<td>68</td>
<td>62</td>
</tr>
<tr>
<td>5' 4&quot;</td>
<td>163</td>
<td>71</td>
<td>66</td>
</tr>
<tr>
<td>5' 5&quot;</td>
<td>165</td>
<td>74</td>
<td>68</td>
</tr>
<tr>
<td>5' 6&quot;</td>
<td>168</td>
<td>77</td>
<td>71</td>
</tr>
<tr>
<td>5' 7&quot;</td>
<td>170</td>
<td>79</td>
<td>74</td>
</tr>
<tr>
<td>5' 8&quot;</td>
<td>173</td>
<td>82</td>
<td>77</td>
</tr>
<tr>
<td>5' 9&quot;</td>
<td>175</td>
<td>85</td>
<td>79</td>
</tr>
<tr>
<td>5' 10&quot;</td>
<td>178</td>
<td>88</td>
<td>82</td>
</tr>
<tr>
<td>5' 11&quot;</td>
<td>180</td>
<td>90</td>
<td>85</td>
</tr>
<tr>
<td>6' 0&quot;</td>
<td>183</td>
<td>94</td>
<td>88</td>
</tr>
<tr>
<td>6' 1&quot;</td>
<td>185</td>
<td>96</td>
<td>90</td>
</tr>
<tr>
<td>6' 2&quot;</td>
<td>188</td>
<td>98</td>
<td>94</td>
</tr>
<tr>
<td>6' 3&quot;</td>
<td>191</td>
<td>101</td>
<td>97</td>
</tr>
<tr>
<td>6' 4&quot;</td>
<td>193</td>
<td>104</td>
<td>99</td>
</tr>
<tr>
<td>6' 5&quot;</td>
<td>195</td>
<td>107</td>
<td>101</td>
</tr>
<tr>
<td>6' 6&quot;</td>
<td>198</td>
<td>109</td>
<td>105</td>
</tr>
<tr>
<td>6' 7&quot;</td>
<td>201</td>
<td>113</td>
<td>108</td>
</tr>
<tr>
<td>6' 8&quot;</td>
<td>203</td>
<td>115</td>
<td>110</td>
</tr>
</tbody>
</table>

Initial Maintenance Dose

Table 2

<table>
<thead>
<tr>
<th>Calculated Creatinine Clearance # (ml/min)</th>
<th>Maintenance Dose</th>
<th>Time after Loading to start maintenance dose (hours)</th>
<th>Recommend ed volume of fluid for each dose</th>
<th>Duration of infusion for each dose</th>
<th>Time of 1st vancomycin pre-dose level**</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 110ml/min</td>
<td>1.5g BD</td>
<td>12</td>
<td>500ml</td>
<td>2.5 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>90 - 110 ml/min</td>
<td>1.25g BD</td>
<td>12</td>
<td>250ml</td>
<td>2.5 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>75 - 89 ml/min</td>
<td>1g BD</td>
<td>12</td>
<td>250ml</td>
<td>2 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>55 – 74 ml/min</td>
<td>750mg BD</td>
<td>12</td>
<td>250ml</td>
<td>1.5 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>40 – 54 ml/min</td>
<td>500mg BD</td>
<td>12</td>
<td>100ml</td>
<td>1 hour</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>30 – 39 ml/min</td>
<td>750mg OD</td>
<td>24</td>
<td>250ml</td>
<td>1.5 hours</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>20 – 29 ml/min</td>
<td>500mg OD</td>
<td>24</td>
<td>100ml</td>
<td>1 hour</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>10 – 19 ml/min</td>
<td>500mg every 48 hours</td>
<td>48</td>
<td>100ml</td>
<td>1 hour</td>
<td>Before 2nd dose</td>
</tr>
<tr>
<td>Oliguric, anuric, or &lt; 10ml/min</td>
<td>Check levels 48 hours after loading dose. Re-dose with 1g once level &lt;15mg/L</td>
<td>Only re-dose once levels &lt;15mg/L</td>
<td>250ml</td>
<td>2 hours</td>
<td>48 hours after dose</td>
</tr>
</tbody>
</table>
# CrCl should be calculated based on the Cockcroft-Gault equation (see section 3.4.1). Using eGFR is not recommended. Note: Use actual body weight or maximum body weight - whichever is lower - to calculate CrCl for vancomycin. In patients with a low creatinine (<60 micromol/L), use 60 micromol/L.

** The loading dose counts as the 1st dose.

**Administration:**
Vancomycin administration must be done slowly at a rate of not more than 10mg/min to prevent infusion-related toxicities.

**Monitoring:**
Pre-dose (‘trough’) serum vancomycin concentrations are the most accurate and practical method of monitoring efficacy.

Samples should be collected immediately pre-dose and the next dose should still be given prior to obtaining the result. Samples for antibiotic assays must NEVER be taken via the intravenous line through which the drug is administered.

The time and date when levels are to be taken must be clearly annotated on the administration section of the prescription and on the level request form.

Renal function (urine output via a fluid balance chart and at least twice weekly U&E’s) should be monitored for patients receiving more than a single dose of vancomycin. Any significant reduction in renal function should lead to repeat U&E’s and a pre-dose vancomycin level just before the next dose is due.

**Target ranges:**
Minimum serum vancomycin trough concentrations should always be maintained above 10mg/L to avoid development of resistance.

It should be noted that it may take up to 5 dosing intervals to achieve steady state levels. When interpreting levels ensure that the 1st pre-dose levels has not been taken too early and that the level you are interpreting is a true pre-dose level and taken at the correct time.

### Maintenance Dose Adjustment using Pre-Dose Steady State Vancomycin Levels
(excluding patients with CrCl <10ml/min, anuric or oliguric – see table 2 for advice on re-dosing)

<table>
<thead>
<tr>
<th>Pre-dose (‘trough’) level</th>
<th>How to adjust the maintenance dose given in Table 2</th>
<th>Time to take subsequent vancomycin level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5mg/L</td>
<td>Increase the dose by two dosing levels (2 rows) from current dosing schedule (e.g. If current dose is 500mg BD, move UP Table 2 by two rows to increase dose to 1g BD)</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>5-10mg/L</td>
<td>Increase dose by one dosing level</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>10-15mg/L</td>
<td>Aiming for 10 - 15mg/L – Continue at current dose</td>
<td>After 3 - 4 days</td>
</tr>
<tr>
<td></td>
<td>Aiming for 15 - 20mg/L – Increase by one dosing level</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>15-20mg/L</td>
<td>Aiming for 10 - 15mg/L – Decrease by one dosing level without omitting any doses (i.e. move DOWN Table 2 by one row)*</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td></td>
<td>Aiming for 15 - 20mg/L – Continue at this dose</td>
<td>After 3 - 4 days</td>
</tr>
<tr>
<td>20-25mg/L</td>
<td>Decrease by one dosing level without omitting any doses*</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>&gt; 25mg/L</td>
<td>Omit next dose. Decrease by two dosing levels*</td>
<td>Before 4th dose</td>
</tr>
<tr>
<td>&gt; 30mg/L</td>
<td>Omit any further doses. Re-check renal function (i.e. U&amp;E’s) and urine output and seek advice from microbiology / pharmacy.</td>
<td>Before 4th dose</td>
</tr>
</tbody>
</table>

* If current regimen is 500mg every 48 hours – seek advice from microbiology / pharmacy

**Refs:**
Thompson et al Development and evaluation of vancomycin dosage guidelines designed to achieve new target concentrations, Journal of Antimicrobial Chemotherapy (2009) 63, 1050-1057

3.4.2.2 Continuous Infusion Vancomycin (Critical Care only)

Vancomycin may be used as a continuous infusion in Critical Care areas. Research has suggested that this is more effective, less toxic and easier to monitor in patients with rapidly fluctuating renal function. Please see Annex 5.

3.4.2.3 Teicoplanin

Teicoplanin levels are not routinely required but monitoring is recommended when prolonged treatment is envisaged e.g. endocarditis, osteomyelitis etc. Trough levels (pre-dose) in excess of 20 mg/L are recommended. Avoid levels >60mg/L.

### ADULTS & ELDERLY PATIENTS WITH NORMAL RENAL FUNCTION

<table>
<thead>
<tr>
<th>Indications</th>
<th>Loading Dose Regimen</th>
<th>Targeted trough concentrations at Day 3 to 5</th>
<th>Maintenance Dose</th>
<th>Targeted trough concentrations during maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated skin and soft tissue infections</td>
<td>400mg iv or im (this equates to approximately 6mg/kg body weight) every 12 hours for 3 administrations</td>
<td>15 - 30mg/L(^2)</td>
<td>6mg/kg body weight iv or im od</td>
<td>&gt;15mg/L(^2) once a week</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>800mg iv (this equates to approximately 12mg/kg body weight) every 12 hours for 3 to 5 administrations</td>
<td>20 - 40mg/L(^2)</td>
<td>12mg/kg body weight iv or im od</td>
<td>&gt;20mg/L(^2) once a week</td>
</tr>
<tr>
<td>Complicated urinary tract infections</td>
<td>800mg iv (this equates to approximately 12mg/kg body weight) every 12 hours for 3 to 5 administrations</td>
<td>30 - 40mg/L(^2)</td>
<td>12mg/kg body weight iv or im od</td>
<td>&gt;30mg/L(^2)</td>
</tr>
</tbody>
</table>

1. In patients with impaired renal function dose adjustment is not required until the 4th day of treatment, at which time dosing should be adjusted.
2. Seek advice from Pharmacy or refer to the SPC for further information.
3. Measured by FPIA

Note: The testing is performed out of county. As such **TESTING IS ONLY POSSIBLE ON A MONDAY TO THURSDAY** and samples **MUST REACH THE LABORATORY** by 1530hrs.

3.4.3 Aminoglycosides

The aminoglycoside antibiotics are potent intravenous antibiotics that can be toxic if misused. The following advice applies equally to GENTAMICIN and TOBRAMYCIN. Amikacin is slightly more complex and should only be used on microbiology advice.

The preferred method of administering these drugs regularly is once daily as supported by the BNF. There are a number of different protocols available but locally we use the Hartford Protocol. This requires a dose of 7mg/kg. **Dosage regimens of 5mg/kg should not be used.**

3.4.3.1 Stat Dosing Of Aminoglycosides

The most common use of aminoglycosides is as a single large dose administered in the acutely ill. The appropriate dose to use, in almost every case, in this circumstance is the large 7mg/kg dose as listed in the table in step 2 below. If only a single dose is planned, levels DO NOT need to be measured.

If a single dose is envisaged but subsequent doses are deemed required, the level must be checked between six and 14 hours post-dose as per section 3.4.3.2.
3.4.3.2 Hartford Aminoglycoside Protocol (Adults)

Recent studies have shown that aminoglycosides can be given as a single dose rather than in divided doses – known as the Hartford regimen. This approach is easier for ward staff, requires fewer levels to be taken and appears to be less nephrotoxic. This regimen gives a standard dose of aminoglycoside (either gentamicin or tobramycin) of 7mg/kg calculated from ideal body weight. A serum level is measured 6-14 hours after the first dose to determine the dosage interval (1).

However this approach is unsuitable for some patients and some conditions and for these cases it will be necessary to use a conventional multiple dose regimen. To ensure that the most appropriate therapeutic regimen is used, follow the steps below:-

**TREATMENT MUST NOT EXCEED 7 DAYS without discussion with Consultant Microbiologist**

**NOTE:** MINIMUM DOSE 320mg MAXIMUM DOSE 560mg

If dose is outside this range, use the Multiple Dosing Aminoglycoside Protocol (Section 3.4.3.3 below)

**STEP 1: IS THE PATIENT SUITABLE?**

**DO NOT USE THIS REGIMEN FOR:**
- Endocarditis
- Urology surgery prophylaxis

Do NOT use this regimen for any of the following, **EXCEPT** on the advice of a Consultant Microbiologist:

- Any patient who has
  - Significant ascites
  - Limb amputation(s)
  - Cystic fibrosis
  - Major burns
  - Renal transplant
  - Renal impairment – creatinine clearance <60mL/min
- Pregnant women
- Children < 16 years

Do not use the automated MDRD eGFR produced by the clinical chemistry laboratory reported on “Ward V”, to calculate dose adjustments in renal impairment. Cockcroft-Gault Creatinine Clearance estimates using the formula listed below

Calculate creatinine clearance (mL/minute):

Men: \[ \frac{1.23 \times (140 – \text{age}) \times \text{Ideal Body Weight in kg}}{\text{Serum creatinine (micromol/L)}} \]

Women: \[ \frac{1.04 \times (140 – \text{age}) \times \text{Ideal Body Weight in kg}}{\text{Serum creatinine (micromol/L)}} \]

**IBW calculations**

Female IBW = 45kg + (2.3kg x no. of inches over 5 feet) using height in feet and inches

or

Female IBW = 45 + (0.91 x (ht. in cm – 152.4))

Male IBW = 50kg + (2.3kg x no. of inches over 5 feet) using height in feet and inches

or

Male IBW = 50 + (0.91 x (ht. in cm – 152.4))

If patient is < 5 feet (< 150cm) tall, use IBW = 45kg (females) or 50kg (males)
STEP 2: CALCULATE THE DOSE

- Determine the patient’s:
  - Gender
  - Height
  - Weight in kg
  (To convert from imperial weight measurements to metric 1 stone = 6.35kg, 1 lb = 0.45kg)

- Read off the patient’s ideal body weight (IBW) for their gender and their height from the appropriate chart below.

- Compare the patient’s actual body weight (ABW) with their ideal body weight (IBW)

- If the patient’s ABW is less than their IBW (i.e. they are underweight), use their ABW to estimate the aminoglycoside dose from the charts below

- If the patient’s ABW is more than, or the same as, their IBW, use their IBW to estimate the aminoglycoside dose from the charts below

Note: Dose should never exceed 560 mg

<table>
<thead>
<tr>
<th>Height</th>
<th>ADULT MALES (&gt;16 yrs)</th>
<th>Height</th>
<th>ADULT FEMALES (&gt; 16 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IBW (kg)</td>
<td>Gentamicin</td>
<td>ABW (use if less than IBW)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tobramycin dose (mg)</td>
<td>(kg)</td>
</tr>
<tr>
<td>6'1&quot; or over</td>
<td>Over 79.9</td>
<td>560</td>
<td>78 – 82</td>
</tr>
<tr>
<td>1.85m or over</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5'10&quot; – 6&quot;</td>
<td>73 – 77.6</td>
<td>520</td>
<td>72 - 77</td>
</tr>
<tr>
<td>1.77 – 1.82m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5’7&quot; – 5’9&quot;</td>
<td>66.1 – 70.7</td>
<td>480</td>
<td>66 - 71</td>
</tr>
<tr>
<td>1.7 – 1.75m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5’5&quot; – 5’6&quot;</td>
<td>61.5 – 63.8</td>
<td>440</td>
<td>60 - 65</td>
</tr>
<tr>
<td>1.65 – 1.68m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5’2&quot; – 5’4&quot;</td>
<td>54.6 – 59.2</td>
<td>400</td>
<td>55 - 59</td>
</tr>
<tr>
<td>1.57 – 1.63m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5’1&quot; or under</td>
<td>Under 52.3</td>
<td>360</td>
<td>49 - 54</td>
</tr>
<tr>
<td>1.55m or under</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5’1&quot; or under</td>
<td>Under 47.3</td>
<td>320</td>
<td>43 - 48</td>
</tr>
<tr>
<td>1.55m or under</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

STEP 3: HOW TO GIVE THE GENTAMICIN or TOBRAMYCIN

- Dilute the antibiotic dose in 100mL sodium chloride 0.9% and give by intravenous infusion over 1 hour.

- Record on the drug chart the exact start time of the infusion.

BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS
STEP 4: HOW TO MEASURE AMINOGLYCOSIDE LEVELS

- The laboratories are able to do assays daily during routine laboratory hours. Take a blood sample at the right time and the sample will be analysed in hours and the result should be available before the next dose is due.

- Do not take the blood sample from the iv line used for aminoglycoside administration.

- Collect one blood sample (ideally 10mL) between 6 and 14 hours after the start of the first infusion in a plain tube (i.e. clotted blood).

- Document on the microbiology request form the exact time and date the infusion was set up (see prescription chart) and the exact time and date the sample was taken in addition to the patient details and Hartford Regimen.

- The specimen bottle must show the:
  - Patient’s name
  - Date of birth
  - Ward
  - Date and time the sample was taken

STEP 5: SELECTING DOSE INTERVAL

When the level is available:-

- Plot the level on the nomogram.

- If the level falls in the area designated 24 hours, 36 hours or 48 hours the dosing interval is 24, 36 or 48 hourly respectively.

- If the level falls on a line between dosing intervals choose the longer interval.

- If the level is above the 48 hour line, STOP the treatment. If the drug is to be continued take daily levels and do not give any more aminoglycoside without first consulting Consultant Microbiologist

STEP 6: REPEATED MONITORING

- U & Es and creatinine need to be checked daily in all patients on the Hartford Regimen.

- Repeat aminoglycoside levels as shown in the table.

- If the serum creatinine is rising significantly (20% or more), and it is still within 6-14 hours of the start of this infusion measure the level as soon as possible. If more than 14 hours contact microbiology or pharmacy for advice.

Reference
(1) Antimicrobial Agents and Chemotherapy March 1995 ; 39 : 650-655
3.4.3.3 Multiple Dosing Aminoglycoside Protocol (Gram negative sepsis)

For patients who are excluded from once-daily dosing protocol, parenteral gentamicin or tobramycin can be given as an intravenous bolus using a multiple dosing regimen (which may be only one dose per day).

**ADULTS**

1. **For normal renal function (GFR >60 mL/min)** give 3-4mg/kg bodyweight as total daily dose given in divided doses usually every 8 to 12 hours. For obese patients remember to use the IBW. See above for IBW calculations.

2. **For impaired renal function** calculate the creatinine clearance (section 3.4.3.2) and use the doses from the table below.

<table>
<thead>
<tr>
<th>Creatinine clearance (GFR) mL/min</th>
<th>Dose and frequency of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 – 60</td>
<td>80mg every 12 hours</td>
</tr>
<tr>
<td>10 – 30</td>
<td>80mg daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>80mg every 48 hours</td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

Each dose can be administered as an undiluted intravenous injection over 2-3 minutes.

**MONITORING LEVELS**

1. In patients with normal renal function, measure serum levels after 3-5 doses.
2. Patients with renal impairment may require more frequent monitoring.
3. Blood samples for levels must not be taken from the site of administration.
4. Pre-dose levels should be taken immediately before the dose is administered (but NOT before the FIRST dose).
5. Post-dose levels should be taken 1 hour after the dose is finished.

**PRE – DOSE (TROUGH) LEVELS**

1. The target range is < 2mg/L to minimise toxicity. Remember that apparently high levels may be due to mistiming of samples.
2. If the level is within target then continue the regimen and continue to monitor twice weekly - so long as renal function is stable.
3. If the pre-dose is between 2-3mg/L (and renal function unchanged) **decrease the frequency** e.g. from every eight hours to every twelve hours.
4. If the pre-dose level is > 3mg/L withhold therapy and discuss with microbiology.

**POST – DOSE (PEAK) LEVELS**

1. For most infections the target range is 5-10mg/L.
2. For serious Gram negative or pseudomonas infections the target range is 7-10mg/L.
3. If the post dose level is below the target range the level is sub-therapeutic and each **dose must be increased** by 40mg.
### 3.4.3.4 Aminoglycoside dosing for Endocarditis, Listeriosis and other complex Gram positive infections

In these conditions, the drug is used for synergy and MUST be given with a cell-wall active agent (i.e. a beta-lactam or a glycopeptide)

1. **For normal renal function** (GFR >60 mL/min) give 1mg/kg bodyweight given every 12 hours. For obese patients remember to use the dose determining weight calculated from IBW - see above.

2. **For impaired renal function** calculate the creatinine clearance (section 3.4.3.2) and use the doses from the table below

<table>
<thead>
<tr>
<th>3. Creatinine clearance (GFR) mL/min</th>
<th>4. Dose and frequency of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 – 60</td>
<td>1 mg/kg IBW (Max 80mg) every 12 hours</td>
</tr>
<tr>
<td>10 – 30</td>
<td>Max 80mg daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Max 80mg every 48 hours</td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

Each dose can be administered as an undiluted intravenous injection over 2-3 minutes.

**MONITORING LEVELS**

1. In patients with normal renal function, measure serum levels after 3-5 doses.
2. Patients with renal impairment may require more frequent monitoring.
3. Blood samples for levels must not be taken from the site of administration.
4. Pre-dose levels should be taken immediately before the dose is administered (but NOT before the FIRST dose).
5. Post-dose levels should be taken 1 hour after the dose is finished.

**PRE – DOSE (TROUGH) LEVELS**

1. The target range is < 1mg/L to minimise toxicity. Remember that apparently high levels may be due to mistiming of samples.

2. If the level is within target then continue the regimen and continue to monitor twice weekly - so long as renal function is stable.

3. If the pre-dose is >1.0mg/L (and renal function unchanged) decrease the frequency e.g. from every eight hours to every twelve hours.

4. If the pre-dose level is > 2mg/L withhold therapy and discuss with microbiology.

**POST – DOSE (PEAK) LEVELS**

1. The target peak level is in the range is 3-5mg/L.

2. If the post dose level is below the target range the level is sub-therapeutic and each dose must be increased by 40mg.
3.4.3.5 Amikacin Once A Day

**Indication**

When no other antibiotic is appropriate – **on advice Path Links Microbiology advice only**, as the Microbiologist will need to confirm there are facilities in place for timely analysis of serum levels, in order to ensure safe and effective treatment.

**Contraindications**

See Under 3.4.3.2: Hartford Aminoglycoside Protocol (Adults)

**Initial Dose**

This must be approximately 15mg/kg body weight amikacin (refer to table below) administered by iv infusion over 1 hour in 100mL of 0.9% sodium chloride or 5% glucose. Doses other than 15mg/kg cannot be interpreted from the nomogram.

The table below may be used to rapidly calculate the dose of amikacin required. It applies to adults only.

Select the patient's height from the left hand column and check that their actual weight is within the range given in the appropriate male or female column. Where the patient's actual body weight (ABW) EXCEEDS their ideal body weight (IBW), use the IBW column. Use ABW column only for underweight/emaciated patients.

The dose and injection volume (of 500mg/2ml strength) is then given in the column to the right of the weight range. This should be diluted in 100ml of 0.9% sodium chloride or 5% dextrose and administered by infusion over one hour.

<table>
<thead>
<tr>
<th>Height</th>
<th>IBW (kg)</th>
<th>Amikacin Dose/volume</th>
<th>ABW (use if less than IBW) (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6'1&quot; or over (1.85m or over)</td>
<td>Over 79.9</td>
<td>1250mg, 5.0ml</td>
<td>78 – 82</td>
</tr>
<tr>
<td>5'10&quot; – 6' (1.77 – 1.82m)</td>
<td>73 – 77.6</td>
<td>1150mg, 4.6ml</td>
<td>72 – 77</td>
</tr>
<tr>
<td>5'7&quot; – 5'9&quot; (1.7 – 1.75m)</td>
<td>66.1 – 70.7</td>
<td>1050mg, 4.2ml</td>
<td>66 - 71</td>
</tr>
<tr>
<td>5'5&quot; – 5'6&quot; (1.65 – 1.68m)</td>
<td>61.5 – 63.8</td>
<td>950mg, 3.8ml</td>
<td>60 - 65</td>
</tr>
<tr>
<td>5'2&quot; – 5'4&quot; (1.57 – 1.63m)</td>
<td>54.6 – 59.2</td>
<td>850mg, 3.4ml</td>
<td>55 - 59</td>
</tr>
<tr>
<td>5'1&quot; or under (1.55m or under)</td>
<td>Under 52.3</td>
<td>750mg, 3.0ml</td>
<td>49 - 54</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Height</th>
<th>IBW (kg)</th>
<th>Amikacin Dose/volume</th>
<th>ABW (use if less than IBW) (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6' 3&quot; (1.9m) or over</td>
<td>79.5</td>
<td>1250mg, 5.0ml</td>
<td>78 - 82</td>
</tr>
<tr>
<td>6' – 6'2&quot; (1.82 – 1.88m)</td>
<td>72.6 – 77.2</td>
<td>1150mg, 4.6ml</td>
<td>72 - 77</td>
</tr>
<tr>
<td>5'10&quot; – 5'11&quot; (1.77 – 1.8m)</td>
<td>68 – 70.3</td>
<td>1050mg, 4.2ml</td>
<td>66 - 71</td>
</tr>
<tr>
<td>5'7&quot; – 5'9&quot; (1.7 – 1.75m)</td>
<td>61.1 – 65.7</td>
<td>950mg, 3.8ml</td>
<td>60 - 65</td>
</tr>
<tr>
<td>5'4&quot; – 5'6&quot; (1.63 – 1.68m)</td>
<td>54.2 – 58.8</td>
<td>850mg, 3.4ml</td>
<td>55 - 59</td>
</tr>
<tr>
<td>5'2&quot; – 5'3&quot; (1.57 – 1.6m)</td>
<td>49.6 – 51.9</td>
<td>750mg, 3.0ml</td>
<td>49 - 54</td>
</tr>
<tr>
<td>5'1&quot; or under (1.55m or under)</td>
<td>Under 47.3</td>
<td>650mg, 2.6ml</td>
<td>43 - 48</td>
</tr>
</tbody>
</table>

**IBW calculations**

Female IBW = 45kg + (2.3kg x no. of inches over 5 feet) using height in feet and inches

or

Female IBW = 45 + (0.91 x (ht. in cm – 152.4))

Male IBW = 50kg + (2.3kg x no. of inches over 5 feet) using height in feet and inches

or

Male IBW = 50 + (0.91 x (ht. in cm – 152.4))

If patient is < 5 feet (< 150cm) tall, use IBW = 45kg (females) or 50kg (males)
Subsequent doses

Do not give a second dose until level is confirmed from the first dose. This will indicate the frequency of dosing as either 24 hourly or less frequently.

To work out dosing interval, plot the amikacin blood level on the nomogram against the time the sample was taken after the start of the infusion. If the level falls in the area designated 24h, 36h or 48hr, the dosing interval is 24, 36 or 48 hourly respectively. For example amikacin drug level concentration is 10mg/L and this was taken 10 hours post infusion, therefore dosing interval is 24 hours.

Note: changes are made in the dosing interval – the dose remains constant at 15mg/kg.

Serum level Monitoring

Take a sample between 6 and 14 hours after the start of the infusion. The following information must be clearly stated on the request form.

- Time infusion started
- Time sample was taken
- Dose administered

Caution with Once daily Amikacin

Renal toxicity with amikacin is more likely in the elderly, those who are septic or on other potentially nephrotoxic drugs e.g.: NSAID, ACE inhibitors or diuretics, regardless of initial creatinine. In such patients, the continued need for amikacin should be reviewed daily and should not generally exceed 3 days.

Once Daily Amikacin Nomogram

- Q24h dose every 24 hours
- Q36h dose every 36 hours
- Q48h dose every 48 hours
3.4.4 Co-trimoxazole

High dose co-trimoxazole therapy e.g. for pneumocystis treatment may occasionally be required. Unlike standard dose therapy, levels may need monitoring. Samples should be collected immediately pre-dose and 1 hour post if iv or 2 hours post-dose if oral.

Pre-dose sulphonamethoxazole levels should be <100mg/L
Post-dose sulphonamethoxazole levels should be between 120 and 150 mg/L

Pre-dose trimethoprim levels should be 5 to 7mg/L
Post-dose trimethoprim levels should be >10mg/L but <20mg/L

**Note:** The testing is performed by an external reference laboratory. As such TESTING IS ONLY POSSIBLE ON A MONDAY TO THURSDAY and samples MUST REACH THE LABORATORY by 1530hrs.

3.4.5 Other Antibiotics Requiring Monitoring

Some other antimicrobials also require levels monitoring and some require monitoring of other markers. The following table is by no means an exhaustive list.

**Note:** Like co-trimoxazole, the testing of drug levels is performed by an external reference laboratory. As such TESTING IS ONLY POSSIBLE ON A MONDAY TO THURSDAY and samples MUST REACH THE LABORATORY by 1530hrs.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>Hepatic function weekly</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>Creatinine kinase initial baseline and weekly thereafter</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Blood pressure for first 24 hours</td>
</tr>
<tr>
<td></td>
<td>Platelet &amp; white blood cell count weekly</td>
</tr>
<tr>
<td></td>
<td>Visual acuity if treating for &gt;14 days.</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Levels may require monitoring</td>
</tr>
<tr>
<td></td>
<td>Trough levels should be &lt;15mg/L</td>
</tr>
<tr>
<td></td>
<td>Peak levels should be 15-25mg/L</td>
</tr>
<tr>
<td>Colistin</td>
<td>If given intravenously pre-dose levels should be in the range of 2-4mg/L. There is no need to monitor post dose levels on standard dosing regimens.</td>
</tr>
</tbody>
</table>
Regimens For Treatment Of Common Infections

Empirical (Blind) Antimicrobial Chemotherapy

The initiation of antimicrobial chemotherapy should normally be withheld until appropriate specimens are collected and a microbiological diagnosis is made unless:

- the patient’s defences are compromised
- a life-threatening infection is clinically evident or suspected
- appropriate laboratory investigations cannot be rapidly performed

In such cases antimicrobial chemotherapy should commence immediately after the collection of the diagnostic specimens.

4.1 Urinary Tract Infections

4.1.1 Tuberculosis, Renal

Specimens: Three consecutive early morning specimens of urine. Seek advice from Consultant Microbiologist.

4.1.2 Uncomplicated Urinary Tract Infections (Simple cystitis)

Note:

1. In long-term catheterised patients only those with relevant clinical signs of infection need treatment.

2. Microscopic examination of urine alone is of limited value in unequivocally diagnosing infection; therefore any such emergency request is not normally entertained.

3. In recurrent prostatitis discuss treatment with Consultant Microbiologist.

First Line: Nitrofurantoin 100mg po every 6 hours
Duration: Females (non-catheterised) 3 days, Males 7 days

NOTE: Nitrofurantoin is both ineffective and toxic in renal failure and is contraindicated in patients with an eGFR <45ml/min. It is also ineffective in complicated UTIs and should only be used in simple cystitis.

Second Line: Trimethoprim 200mg po every 12 hours
Duration: Females (non-catheterised) 3 days, Males 7 days

Third Line: Co-amoxiclav 625mg po every 8 hours
Duration: Females (non-catheterised) 3 days, Males 7 days.

In pregnancy, trimethoprim is contra-indicated in first and second trimester—amoxicillin (only to be used if organism known to be sensitive) or co-amoxiclav should be first choice.

Second line in pregnancy:

First trimester: Trimethoprim is absolutely contra-indicated. Drugs of choice are nitrofurantoin or co-amoxiclav or cefalexin.

Second trimester: Trimethoprim is relatively contra-indicated. Drugs of choice are nitrofurantoin or co-amoxiclav or cefalexin.

Third trimester: Nitrofurantoin should be avoided at term. Drugs of choice are trimethoprim or co-amoxiclav or cefalexin.
Take an MSU for culture and sensitivity, and change treatment according to sensitivity, as pyelonephritis is relatively common in pregnancy.

4.1.3 Uncomplicated Urinary Tract Infections, Acute, Hospital-Acquired

1. In catheterised patients, antibiotic therapy is unlikely to eliminate colonising microorganisms. Such organisms are, however, always identified and their antibiograms recorded in case sepsicaemia develops.
2. Short-term urinary catheters must be removed as soon as possible.
3. Seek microbiological advice.

**First Line:** Trimethoprim 200mg po every 12 hours
**Duration:** 7 days

**Second Line:** Gentamicin (7mg/kg ideal body weight, frequency according to Hartford Nomogram) see section 3.4.3.2.
**Duration:** 3 days

4.1.4 Lower Urinary Tract Infections, Chronic

**Note:**

1. Antibiotic therapy in catheterised patients is unlikely to eliminate the microorganisms colonising the catheter, which should be removed as soon as possible. Patients with a long-term catheter should be treated only if symptomatic and/or with significant ascending infection.
2. In the asymptomatic catheterised patient, mixed growth of microorganisms, even in the presence of white cells, does not warrant antibiotic therapy.
3. Long-term antimicrobial prophylaxis is ineffective and promotes resistance so should NOT be used. Discuss with Consultant Microbiologist before embarking on this.

**First Line:** Contact Consultant Microbiologist

4.1.5 Complicated Urinary Tract Infection inc. Pyelonephritis

Consider need for stat dose of gentamicin (see section 3.4.3.1) if signs of systemic sepsis

**First Line:** Co-amoxiclav 1.2g iv every 8 hours with oral switch when appropriate
**Duration:** 7-10 days

**Second Line** (Beta-lactam allergy):

**Duration:**

**Third Line** (Beta-lactam allergy):

**Duration:**

Gentamicin (7mg/kg ideal body weight, frequency according to Hartford Nomogram) see section 3.4.3.2.
**Duration:** 7 days
4.1.6 Acute Prostatitis

First Line: Piperacillin/tazobactam 4.5g iv every 8 hours plus gentamicin 7mg/kg iv at a frequency according to the Hartford Nomogram (see section 3.4.3.2)

Duration: 5 days

And then manage as chronic prostatitis below

Second Line (Beta-lactam allergy):

Contact Consultant Microbiologist

4.1.7 Chronic Prostatitis

First Line: Trimethoprim 200mg po every 12 hours

Duration: 28 days

Second Line: Ciprofloxacin 500mg po every 12 hours

Duration: 28 days

Review by Consultant Urologist required with regard to need to prolong course for further 2-4 weeks.

4.1.8 Epididymo-orchitis

See 4.7.4

4.2 Upper Respiratory Tract Infections

4.2.1 Common Cold

Viral condition – symptomatic treatment only.

4.2.2 Influenza

Annual vaccination is the most effective way of preventing influenza and should be offered to all “at-risk” patients in accordance with national guidelines.

For otherwise healthy adults, the use of zanamivir or oseltamivir is not recommended. Zanamivir or oseltamivir are recommended when influenza is circulating in the community, for the treatment of “at-risk” adults presenting with symptoms of influenza-like illness (ILI) who can commence treatment within 48 hours of the start of symptoms. See Appendix 2.

4.2.3 Mastoiditis, Chronic

Seek advice from ENT Surgeons.

4.2.4 Otitis Externa, Infective

NB in the presence of infection do not use steroids alone. Keep dry.

First Line: AURAL TOILET
4.2.5 Malignant Otitis Externa

Referral to ENT is advised

First Line: Piperacillin/tazobactam 4.5g iv every 8 hours, changing to ciprofloxacin 750mg po every 12 hours once the patient is stable
Duration: 10-14 days total

Second Line (Beta-Lactam allergy): Contact Consultant Microbiologist

4.2.6 Otitis Media, Acute

Most cases of this are viral

First Line: Analgesics/anti-inflammatories only
Duration: 3 days – thereafter treat as chronic.

4.2.7 Otitis Media, Chronic

Referral to ENT is advised

First Line: Amoxicillin 500mg po every 8 hours
Duration: 5 days

Second Line (Beta-lactam allergy): Clarithromycin 500mg po every 12 hours
Duration: 5 days

4.2.8 Peritonsillar Abscess (Quinsy)

First Line: Benzylpenicillin 1.2g iv every 4 hours for 3 days, thereafter amoxicillin 500mg po every 8 hours for 5 days
Second Line (Beta-lactam allergy): Consult Consultant Microbiologist.

4.2.9 Sore Throat/ Pharyngitis /Tonsillitis

The majority of sore throats are viral in aetiology and most patients will not benefit from antibiotics. However, it is difficult to distinguish between viral and streptococcal infections. Patients with 3 of 5 Centor criteria (history of fever, purulent tonsils, cervical adenopathy, absence of cough) or history of otitis media may benefit more from antibiotics. Seven days treatment ensures less frequent relapse than three days. Prescribing antibiotics for sore throat only marginally affects the resolution of symptoms even for those identified as requiring antibiotics through Centor criteria risk assessment. Antibiotics only reduce symptoms by 8 hours. Strategies for delayed or post-dated prescriptions should be considered for this group.

NB for severe infections, parenteral antibiotics may be required in which case treat as Quinsy above. Beware Epstein-Barr virus infection can also present this way and this is a contraindication to Amoxicillin containing products like Co-amoxiclav.
Antibiotic Formulary Prescribing Advice Adult V7.1.docx
Printed copies are not controlled and are valid on date of printing only. This version was last printed: 15/12/2016

Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications.

**First Line:** Phenoxymethylpenicillin 500mg po every 6 hours
**Duration:** 10 days.

**Second Line (Beta-lactam allergy):** Clarithromycin 500mg po every 12 hours
**Duration:** 10 days

**Second Line (Failed therapy):** Co-amoxiclav 625mg po every 8 hours
**Duration:** 7 days

### 4.2.10 Epiglottitis

**First Line:** Cefotaxime 2g iv every 8 hours
**Duration:** 7 days

**Second Line (Beta-lactam allergy):** Contact Consultant Microbiologist

### 4.2.11 Sinusitis, Acute

Most cases of this are viral

**First Line:** Analgesics/anti-inflammatories only
**Duration:** 3 days – thereafter treat as chronic.

### 4.2.12 Sinusitis, Chronic

**First Line:** Co-amoxiclav 625mg po every 8 hours
**Duration:** 5 days.

**Second Line (Beta-lactam allergy):** Doxycycline 100mg po every 12 hours
**Duration:** 5 days

**Third Line:** Clarithromycin 500mg po every 12 hours
**Duration:** 5 days

Seek ENT advice if complex or not responding

### 4.2.13 Tonsillitis (see Pharyngitis)

### 4.2.14 Whooping Cough

**NB: This is a notifiable condition.**

Antibiotics have little effect if administered in the paroxysmal stage.

**First Line:** Clarithromycin 500mg po every 12 hours
**Duration:** 10 days

**Second Line:** Discuss with Consultant Microbiologist
4.3 Lower Respiratory Tract Infections Inc. COPD, Pneumonia, TB

4.3.1 Bronchitis, Acute

First Line: Symptomatic relief only  
Duration: 3 days – thereafter treat as chronic

4.3.2 Bronchitis, Chronic And COPD, Acute Exacerbations Of

First Line: Doxycycline 200mg loading dose on day 1, then 100mg od po from day 2  
Duration: 5 days

Second Line: Amoxicillin 500mg po every 8 hours  
Duration: 5 days

Third Line: Clarithromycin 500mg po every 12 hours  
Duration: 5 days

4.3.3 Pneumonia

Introduction

Specimens: fresh sputum and blood for culture; blood for serology should be collected at onset of disease, and two weeks later.

If patient apyrexial for at least 24 hours you may change the route to oral.

The following advice has been adapted from the current NICE Guidelines (CG191) on the management of community-acquired pneumonia in adults admitted to hospital taking into account the increased risk of *Clostridium difficile*, MRSA and other hospital acquired complications.

4.3.4 Community Acquired Pneumonia

CURB-65 (British Thoracic Society)  
NOTE: Clinical or X-ray evidence of lobar consolidation required.

Score 1 for each

- acute unexplained Confusion (mental test score <8, or disorientation in time/place/person)
- Urea > 7mmol/l
- Respiratory rate ≥30/min
- Blood pressure – systolic <90 mmHg and/or diastolic ≤60 mmHg
- Age 65 years or over

THE CURB-65 SCORE IS NOT A SUBSTITUTE FOR GOOD CLINICAL JUDGEMENT

Mild Pneumonia (CURB Score 0-1)

First Line: Amoxicillin 500mg-1g po every 8 hours  
Duration: 5 days

Second Line: Doxycycline 200mg loading dose on day 1, then 100mg od po from day 2  
Duration: 5 days

Third Line: Clarithromycin 500 mg po 12 hourly  
Duration: 5 days
NICE CG191 suggests ‘Consider extending the course of the antibiotic for longer than 5 days as a possible management strategy for patients with low-severity community-acquired pneumonia whose symptoms do not improve as expected after 3 days.’ This is for generally community patients who should be advised to report back if no real benefit seen within 3 days, but the same principle of extending course duration would apply in the hospital setting too.

Note: The first line choice does not cover atypical pathogens. Most of these are self-limiting infections but should be considered in cases of treatment failure

**Moderate Pneumonia** (CURB Score 2)

**First Line:** Amoxicillin 500mg - 1g po every 8 hours **plus**
clarithromycin 500mg po every 12 hours

**Duration:** 7 days

**Second Line (Beta-lactam allergy):** Doxycycline 100mg po every 12 hours
OR
Clarithromycin 500mg po every 12 hours

**Duration:** 7 days

**Third Line:** Discuss with Consultant Microbiologist

**Severe Pneumonia** (CURB Score ≥3 or Pa O$_2$ <8 KPa or Sa O$_2$ <92% on any Fi O$_2$)

Duration of therapy is usually 7 to 10 days but contact microbiology if no significant response to therapy after 72 hours, suspicion of PVL or other unusual organism.

**First Line:** Co-amoxiclav* 1.2g iv every 8 hours **plus** clarithromycin
500mg iv or po every 12 hours. Consider early oral switch for clarithromycin.

**Duration:** 7 - 10 days

**Second Line:** If penicillin allergy but can tolerate cefuroxime: cefuroxime
1.5g iv every 8 hours **plus** clarithromycin 500mg iv or po every 12 hours. Consider early oral switch for clarithromycin.

**Duration:** 7 - 10 days

**Third Line:** Discuss with Consultant Microbiologist

* Consider additional amoxicillin. See section 3.2.

**NOTE:** Clarithromycin is aimed at atypical organisms and its use with a Beta-lactam carries a significant Clostridium difficile risk. Furthermore, as a bacteriostatic agent, it may act to antagonise the action of the bactericidal Beta-lactam antibiotic. **ENSURE THE MACROLIDE IS REALLY NECESSARY!** Clarithromycin should be stopped once atypical pneumonia is excluded.

**Atypical Pneumonia**

Treatment must be directed at the causative agent and may need to be prolonged. Consider underlying disease processes (e.g. need for HIV test).

If there are problems with antibiotic allergy, and/or concerns about the response to the above antibiotics, please contact the duty Microbiologist for your site.
4.3.5 Hospital-Acquired Pneumonia
(NB: Respiratory samples are essential.)

Early onset (<5 days admission, no antibiotics within the last 7 days):

Mild
First Line: **Doxycycline** 100mg po every 12 hours
Duration: Review at 5 days
Second Line: **Amoxicillin** 500mg-1g po every 8 hours
Duration: Review at 5 days
Third Line: Discuss with Consultant Microbiologist

Moderate
First Line: **Co-amoxiclav** 1.2g iv every 8 hours. Review daily with a view to early iv to oral switch.
Duration: Review at 5 days
Second Line (Minor penicillin rash): **Cefuroxime** 1.5g iv every 8 hours.
Duration: Review at 5 days
Third Line: Discuss with Consultant Microbiologist
(Severe Beta-lactam allergy/MRSA risk): *Consider additional amoxicillin. See section 3.2.

Late onset (>5 days admission and antibiotics within the last 7 days) or severe:
First Line: **Piperacillin/tazobactam** 4.5g iv every 8 hours
(if severe HAP, increase frequency to every 6 hours)
Second Line (Minor penicillin rash): **Meropenem** 1g iv every 8 hours
Third Line (Severe Beta-lactam allergy/MRSA risk): Discuss with Consultant Microbiologist
Duration At least 5 days treatment, but seek advice from on-call Consultant Microbiologist if no significant improvement at 72 hours

4.3.6 Pneumonia, Aspiration

NB This is not appropriate for aspiration in the absence of pneumonia.
First Line: **Co-amoxiclav** 1.2g iv every 8 hours
Duration: 5 days. Consider oral therapy if patient’s condition permits.
Second Line (Minor penicillin rash): **Cefuroxime** 1.5g iv every 8 hours plus **metronidazole** 500mg iv every 8 hours
Duration: 5 days
Third Line: (Severe beta-lactam allergy/MRSA risk): Discuss with Consultant Microbiologist.
4.3.7 Empyema or Lung Abscess

**NB:** Endeavour to isolate infective agent before attempting antimicrobial therapy.

Contact Consultant Microbiologist

4.3.8 Bronchiectasis

Consultant local Chest Physicians or the [BTS Guidelines](#).

4.3.9 Tuberculosis

**NB:** Isolate patient until non-infective.

Contact Consultant Chest Physician for advice.

4.4 Soft Tissue Infections

4.4.1 Bed Sores (See Ulcers)

4.4.2 Bites

4.4.2.1 Minor Bites

- **First Line:** Co-amoxiclav 625mg po every 8 hours
- **Duration:** 7 days

- **Second Line (Beta-lactam allergy):** Doxycycline 100mg po every 12 hours plus metronidazole 400mg po every 8 hours
- **Duration:** 7 days

**Human bites:** Consider risks of blood borne viral infection eg Hepatitis B, C and HIV.

**Exotic animal bites or bites sustained overseas:** Consider Rabies risk.

Consider **Tetanus immune status** – is further vaccination/immunoglobulin required?

4.4.2.2 Severe Bites

**NB Surgical debridement is mandatory**

- **First Line:** Co-amoxiclav 1.2g iv every 8 hours
- **Duration:** Review regularly with a view to oral switch

- **Second Line (Beta-lactam allergy):** Ciprofloxacin 400mg iv every 12 hours plus Clindamycin 900mg iv every 8 hours.
- **Duration:** Review regularly with a view to oral switch

**Human bites:** Consider risks of blood borne viral infection eg Hepatitis B, C and HIV.

**Exotic animal bites or bites sustained overseas:** Consider Rabies risk.

Consider **Tetanus immune status** – is further vaccination/immunoglobulin required?
4.4.3 Boils

*NB:* No antibiotic therapy is indicated, unless there are signs of cellulitis (see below), or if the patient is immunocompromised. Consult Consultant Microbiologist.


4.4.4 Burns (Uncomplicated)

Routine use of systemic antibiotics is **NOT** indicated.

4.4.5 Surgical Site Infections

*First Line:* **Co-amoxiclav** 625mg po every 8 hours. Consider need for additional amoxicillin. See Section 3.2.

*Duration:* 5 days

*Second Line (Beta-lactam allergy):** **Clindamycin** 450mg po every 6 hours.

*Duration:* 5 days

*Third Line: (MRSA risk):* Treat according to susceptibility pattern.

4.4.6 Cellulitis

*Note:* Bilateral cellulitis is **very** uncommon. Such cases usually turn out to be varicose eczema or underlying vascular insufficiency. Seek senior clinical review.

Management - see algorithm below.

4.4.6.1 Cellulitis associated with fresh water immersion

As algorithm but **add ciprofloxacin** 500mg po every 12 hours.

4.4.6.2 Cellulitis associated with salt water immersion

As algorithm but **add doxycycline** 100mg po every 12 hours.
BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS
4.4.7  Necrotising Fasciitis (inc Fournier’s & Synergistic Gangrene)

**NB:** **URGENT Surgical debridement is mandatory**
Consultant Microbiologist input is essential

*First Line:* **Meropenem** 2g iv every 8 hours plus **clindamycin** 1.2g iv every 6 hours

*Second Line (Beta-lactam allergy):* Contact Consultant Microbiologist

4.4.8  Ulcers and other chronic, stable wounds

Antibiotics have no place in the management of chronic, stable wounds.

There is a large group of wounds (surgical or non-surgical) that are swabbed routinely which share a common pathophysiology. When wounds are more than a month old, they are known as chronic or established wounds because they develop a thick, avascular fibrous tissue layer through which underlying bacteria cannot get out and antibiotics cannot easily permeate. Such chronic wounds include:

- Chronic ulcers (including varicose leg ulcers and pressure sores)
- Post-surgical wounds more than a month old
- Sinuses and fistulae
- Stoma sites (colostomy, urostomy, etc)

The above wounds will be colonised either with the patients’ own flora or environmental organisms. Swabs taken from such wounds will *always* have growth and, as such, these lesions should not be swabbed (even if purulent). **They should NOT be treated with antibiotics.** Treatment of these cases will result in the emergence of antibiotic resistance. Wound debridement or cleaning without antibiotics will promote healing in most cases.

The complications of ulcers (cellulitis, osteomyelitis, etc) should be managed as normal but it must be understood that antibiotic treatment is being given for these complications **not** for the ulcer or wound. For this reason, the use of topical antibiotics is strongly discouraged.

4.4.9  Diabetic Foot

These must be referred to the diabetic team for review as soon as practicable. A formal MDT may be necessary.

**Uninfected:** IDSA Grade 1

Foot wound not clinically infected ie no pus, erythema, pain, tenderness, warmth or induration.

*First Line:* Symptomatic treatment only.

**Mild Infection:** IDSA Grade 2

Indicated by the presence of ≥ 2 manifestations of inflammation (pus, erythema, pain, tenderness, warmth, or induration), but any cellulitis/erythema extends ≤ 2 cm around the ulcer, and infection is limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness.
Antibiotic Formulary Prescribing Advice Adult V7.1.docx
Printed copies are not controlled and are valid on date of printing only. This version was last printed: 15/12/2016

BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS

**First Line:**
Flucloxacillin 1g po every 6 hours

**Duration:**
5 – 7 days

**Second Line (Beta-lactam allergy):**
Doxycycline 100mg po every 12 hours OR Clindamycin 450mg po every 6 hours

**Duration:**
5 – 7 days

**If MRSA infection suspected**
Contact microbiology for advice

**Moderate Infection:** IDSA Grade 3

Infection as above in a patient who is systemically well, metabolically stable but who one or more of the following; cellulitis extending to > 2 cm, lymphangitis, spread beneath the superficial fascia, deep tissue abscess, gangrene, or involvement of muscle, tendon, joint or bone. Surgical opinion required. Debridement of infected bone is essential for successful treatment.

**First Line:**
If no antibiotics within 90 days flucloxacillin 2g iv every 6 hours plus metronidazole 400mg po every 8 hours OR Co-amoxiclav 1.2g iv every 8 hours

**Duration:**
Review after 5 – 7 days

**Second Line (Beta-lactam allergy):**
Clindamycin 450mg po iv every 6 hours

**Duration:**
Review after 5 – 7 days

**If MRSA infection suspected**
Contact microbiology for advice

**Severe Infection:** Grade 4

Is infection in a patient with systemic toxicity (e.g. fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycaemia, or uraemia). This includes any patient with critical ischemia of the limb. Urgent iv antibiotics and surgical opinion are essential. Debridement of infected bone is required for successful treatment.

**First Line:**
Consider gentamicin 7mg/kg iv STAT if signs of shock. Piperacillin/tazobactam 4.5g iv every 8 hours

**Duration:**
10 - 14 days initially

**Second Line (Beta-lactam allergy):**
Clindamycin 450mg po (or 600mg iv) every 6 hours plus Ciprofloxacin 500mg po (400mg iv) every 12 hours

**Duration:**
10 - 14 days initially

**If MRSA infection suspected**
Daptomycin 6mg/kg iv od OR Vancomycin iv (dose as per 3.4.2.1) plus Ciprofloxacin 500mg po (400mg iv) every 12 hours

**Duration:**
10 - 14 days initially

**4.4.10 Breast Abscesses**

**Lactational Abscess/Mastitis**

**First Line:**
Flucloxacillin 500mg po every 6 hours

**Duration:**
7-10 days

**Second Line (Beta-lactam allergy):**
Erythromycin 500mg po every 6 hours OR Clarithromycin 500mg po every 12 hours (stop breast-feeding)

**Duration:**
7-10 days
Non-Lactational

First Line: Co-amoxiclav 625mg po every 8 hours
Duration: 5 days

Second Line (Beta-lactam allergy): Ciprofloxacin 500mg po every 12 hours plus Metronidazole 400mg po every 8 hours
Duration: 5 days

4.5 Central Nervous System

4.5.1 Brain Abscesses

First Line: Meropenem 2g iv every 8 hours plus metronidazole 500mg iv every 8 hours plus rifampicin 600mg iv every 12 hours and refer to Neurosurgeon

If previous neurosurgery involving implants, add vancomycin (see Section 3.4.2.1)

4.5.2 Meningitis (Aetiology Unknown)

NB: treatment should not be withheld in suspected cases of bacterial meningitis whilst laboratory specimens are collected.

Pre-admission Treatment: Benzylpenicillin 1.2g iv stat adjusted for age

First Line: Cefotaxime 2g iv every 6 hours

(Ceftriaxone 2g iv every 12 hours may be used instead once diagnosis is confirmed.)

Second Line (Severe Beta-lactam allergy): Contact Consultant Microbiologist

If penicillin resistant streptococcus pneumoniae is suspected or if patient is recently returned from areas where this is prevalent (e.g. Spain, South East Asia, USA)

ADD Vancomycin iv (dose as per 3.4.2.1), plus rifampicin 600mg iv/orally every 12 hours

If age is greater than 55 or in presence of significant immunocompromise:

ADD Amoxicillin 2g iv every 4 hours

Second Line (Beta-lactam allergy): Co-trimoxazole 1.44g iv every 12 hours

If signs of encephalitis:

ADD Aciclovir 10mg/kg iv every 8 hours
4.5.3 Meningitis (Meningococcal)

First Line: Benzylpenicillin 1.8g iv every 4 hours
Duration: 5 – 7 days

Second Line
(Minor penicillin rash):
Cefotaxime 2g iv every 6 hours

(Ceftriaxone 2g iv every 12 hours may be used instead once diagnosis is confirmed.)

Duration: 5 – 7 days

Third Line: Contact Consultant Microbiologist
(Severe Beta-lactam allergy)

4.5.4 Meningitis (Pneumococcal)

First Line: Benzylpenicillin 1.8g iv every 4 hours
plus
*Vancomycin iv (dose as per 3.4.2.1)
plus
*Rifampicin 600mg iv or po every 12 hours

Duration: 10 – 14 days

Second Line
(Minor penicillin rash):
Cefotaxime 2g iv every 6 hours

(Ceftriaxone 2g iv every 12 hours may be used instead once diagnosis is confirmed.)
plus
*Vancomycin iv (dose as per 3.4.2.1)
plus
*Rifampicin 600mg iv or po every 12 hours

* Vancomycin and rifampicin may be discontinued once susceptibility of pneumococcus to beta-lactams is confirmed.

Duration: 10 – 14 days

Third Line: Contact Consultant Microbiologist
(Severe Beta-lactam allergy)

4.5.5 Meningitis (Haemophilus)

First Line: Cefotaxime 2g iv every 6 hours

(Ceftriaxone 2g iv every 12 hours may be used instead once diagnosis is confirmed.)

Duration: 7 – 10 days

Second Line: Contact Consultant Microbiologist
(Severe Beta-lactam allergy)
4.5.6 Meningitis (Listeria)

First Line: Amoxicillin 2g iv every 4 hours plus gentamicin 160mg iv every 12 hours - adjust according to levels (see section 3.4.3.4)

Duration: 21 days

Second Line (Beta-lactam allergy): Co-trimoxazole 1.44g iv every 12 hours

Duration: 21 days

4.5.7 Meningitis (viral)

Do not start antivirals routinely.

First Line: Aciclovir 10-15mg/kg ideal body weight iv every 8 hours

Duration: 14 days

Oral aciclovir is inadequate for treating CNS infections

4.5.8 CSF Leak

First Line: Antibiotics NOT routinely indicated.

(Ref: Lancet 1994:344, 1547 – 1551)

4.5.9 Encephalitis (viral)

First Line: Aciclovir 10-15mg/kg ideal body weight iv every 8 hours

Duration: 14 – 21 days

Oral aciclovir is inadequate for treating CNS infections

Note: Herpes virus PCR must be repeated at 14 days. Antivirals may be stopped after 14 days if the routine repeat PCR is negative.

4.6 Gastrointestinal: Food Poisoning and Intra Abdominal Infection

4.6.1 Cholecystitis (Inc Ascending Cholangitis)

First Line: Piperacillin/tazobactam 4.5g iv every 8 hours

Duration: 5 days (Review daily for iv to oral switch to co-amoxiclav)

Second Line (Beta-lactam allergy): Ciprofloxacin 400mg iv every 12 hours plus metronidazole 500mg iv every 8 hours

Duration: 5 days (Review daily for iv to oral switch)

Third Line: Contact Consultant Microbiologist

4.6.2 Diarrhoea (Regardless Of Cause), Gastroenteritis

NB Refrain from prescribing antimicrobial therapy, unless systemic invasion is suspected. Consult Microbiologist. See: Clostridium difficile
4.6.3 Peritonitis (Surgical Abdomen Inc Appendicitis & Diverticulitis)

First Line: Co-amoxiclav 1.2g iv every 8 hours. Consider addition of Metronidazole 500mg iv every 8 hours if co-amoxiclav alone not effective. (Review daily for iv to oral switch)

Duration: Review after 5 days

Second Line (Minor penicillin rash): Cefuroxime 1.5g iv every 8 hours plus metronidazole 500mg iv every 8 hours

Duration: Review after 5 days

Third Line (Severe Beta-lactam allergy): Vancomycin iv (dose as per 3.4.2.1) plus metronidazole 500mg iv every 8 hours plus gentamicin (7mg/kg ideal body weight, frequency according to Hartford Nomogram). Substitute ciprofloxacin 400mg iv every 12 hours for the gentamicin if concerned about nephrotoxicity or AKI.

Duration: Review after 5 days

4.6.4 Gl Bleed Secondary To Hepatic Cirrhosis

First Line: Piperacillin/tazobactam 4.5g every 8 hours iv

Second Line (Beta-lactam allergy): Ciprofloxacin 500mg po every 12 hours or Ciprofloxacin 400mg iv every 12 hours

Duration: 7 days

4.6.5 Spontaneous Bacterial Peritonitis (Hepatic Failure)

(ie ascitic fluid, total white cell count >0.5 x 10^9 or neutrophil count >0.25) (BSG 2006)

First Line: Meropenem 1g iv every 8 hours

Duration: 5 days

Second Line (Severe Beta-lactam allergy): Discuss with Consultant Microbiologist

4.6.6 Acute Pancreatitis

The evidence for antibiotic prophylaxis against infection of pancreatic necrosis is conflicting and difficult to interpret and is not, therefore, recommended.

4.6.7 Hepatic Abscess

NB Drainage, where possible, is essential

First Line: Co-amoxiclav 1.2g every 6 to 8 hours iv. Consider need for additional amoxicillin (See Section 3.2)

Second Line (Beta-lactam allergy): Ciprofloxacin 500mg po (400mg iv) every 12 hours plus Metronidazole 500mg iv every 8 hours

Duration: Review after 7 days. Prolonged treatment may be necessary

4.6.8 Antibiotic (Clostridium difficile) Associated Diarrhoea

NB: Maintain hydration, electrolytes and nutritional intake. Review ALL antimicrobial use. If other diagnoses require antibiotic use, discuss with Consultant Microbiologist.
Severe CDI evaluation based only on the number of diarrhoeal stools may suffer from difficulties in recording such episodes, especially in elderly patients with faecal incontinence. Furthermore, severe CDI may occasionally be characterised by ileus with no diarrhoea. Clinicians need to be alert to the possibility of severe CDI.

See over for treatment algorithm.
**Clostridium difficile Treatment**

**FIRST EPISODE**

If clinically appropriate, discontinue non-\(C.\) \(d\)ifficile antibiotics to allow normal intestinal flora to be re-established. Review PPIs. Suspected cases must be isolated.

**MILD DISEASE**

Conservative management only.

**DAILY ASSESSMENT**

Symptoms improving?

**YES**

Symptoms improving?

**NO**

**MODERATE DISEASE**

Oral metronidazole 400mg every 8 hours for 10-14 days.

**DAILY ASSESSMENT**

Symptoms improving?

**YES**

Encourage Oral intake. Diarrhoea should resolve in 1-2 weeks.

**NO**

**SEVERE DISEASE**

Oral vancomycin 125mg every 6 hours for 10-14 days.

**DAILY ASSESSMENT**

Symptoms worsening?

**YES**

Encourage Oral intake. Diarrhoea should resolve in 1-2 weeks.

**NO**

1\(^{st}\) relapse

Symptoms not improving or worsening. Should not normally be deemed a treatment failure until day 7 of treatment unless evidence of severe CDI: WCC >15, acute rising creatinine and/or signs/symptoms of colitis.

**2\(^{nd}\) or subsequent relapse

Individualised patient management plan required. URGENT Multi-disciplinary review (including Microbiology & Surgery) required.

**RELAPSE**

Diarrhoea AND one of the following: Positive \(C.\) \(d\)ifficile toxin test OR Results of \(C.\) \(d\)ifficile toxin test pending AND clinical suspicion of CDI.

**MUST** discontinue non-\(C.\) \(d\)ifficile antibiotics if at all possible to allow normal intestinal flora to be re-established. Review all drugs with gastrointestinal activity or side effects esp. PPIs & opiates. (Stop PPIs unless required acutely.) Suspected cases must be isolated.

Symptoms/signs of severe CDI:

- WCC >15
- Acute rising creatinine
- Abdominal or radiological signs of Colitis

**Diarrhoea** AND one of the following:

- Positive \(C.\) \(d\)ifficile toxin test
- Results of \(C.\) \(d\)ifficile toxin test pending
- Clinical suspicion of CDI

Diarrhoea should resolve in 1-2 weeks.
4.7 Genital Tract

4.7.1 Pelvic Inflammatory Disease

First Or Second Attack In The Sexually Active (BASHH 2005)

Out-Patient Regimen

First Line: Ceftriaxone 500mg im stat then doxycycline 100mg po every 12 hours, plus metronidazole 400mg po every 12 hours

Second Line (Only if im injection is contraindicated or refused by patient): Cefixime 400mg po stat followed by doxycycline 100mg every 12 hours plus metronidazole 400mg po every 12 hours for 14 days

Caution: Tetracyclines are contra-indicated in pregnancy; instead prescribe clindamycin as in second choice below. Avoid metronidazole in first trimester.

In-Patient Regimen

First Line: Ceftriaxone 2g iv stat then doxycycline 100mg po every 12 hours, plus metronidazole 400mg po every 12 hours

Duration: 14 days

Caution: Tetracyclines are contra-indicated in pregnancy; instead prescribe clindamycin as in second choice below. Avoid metronidazole in first trimester. Quinolones should be avoided in pregnancy.

Second Line (Beta-lactam allergy): Clindamycin 900mg iv every 8 hours for 24 hours plus gentamicin 7mg/kg stat followed by either doxycycline 100mg po every 12 hours plus metronidazole 400mg po every 12 hours or clindamycin 450mg po every 6 hours

Duration: 14 days (Contact microbiology if no response after 48 hours)

Third Line: Ofloxacin 400mg iv every 12 hours plus metronidazole 500mg iv every 8 hours - consider early oral switch

Duration: 14 days (Contact microbiology if no response after 48 hours)

Pelvic Inflammatory Disease at Any Age Following Pelvic/Abdominal Surgery or when STI not suspected

First Line: Co-amoxiclav 1.2g iv, every 8 hours

Duration: 7 days

Second Line (Minor penicillin rash): Cefuroxime 1.5g iv every 8 hours plus metronidazole 500mg iv every 8 hours plus gentamicin 7mg/kg frequency according to Hartford Nomogram (See section 3.4.3.2)

Duration: 7 days

Third Line (Severe Beta-lactam allergy): Consult Consultant Microbiologist
4.7.2 Puerperal Sepsis Or Septic Abortion

**First Line:** Co-amoxiclav 1.2g iv every 8 hours
Duration: 7 days

**Second Line**
(Minor penicillin rash):

Cefuroxime 1.5g iv every 8 hours **plus metronidazole** 500mg iv every 8 hours **plus gentamicin** 7mg/kg frequency according to Hartford Nomogram (See section 3.4.3.2)
Duration: 7 days

Third Line
(Severe Beta-lactam allergy):
Consult Consultant Microbiologist

4.7.3 Chorio-amnionitis

**Known To Be Due To Group B streptococcus**

**First Line:** Benzylpenicillin 1.2g iv every 4 hours
Duration: 7 days (oral switch may be possible after 2 days)

**Second Line**
(Beta-lactam allergy):

Clindamycin 900mg iv every 8 hours
Duration: 7 days (oral switch may be possible after 2 days)

If patient does not show clinical improvement within 12 – 24 hours or deteriorates, switch to regimen given below

**Unknown Organism**

**First Line:** Co-amoxiclav 1.2g iv **plus amoxicillin** 1g iv every 6 hours

Second Line
(Minor penicillin rash):

Cefuroxime 1.5g iv every 8 hours **plus metronidazole** 500mg iv every 8 hours

Third Line
(Severe Beta-lactam allergy):
Contact Consultant Microbiologist.

Duration: Review after 48 hours with view to oral switch. Antibiotics to continue for 7 – 10 days.

4.7.4 Sexually-Transmitted Infections Suspected

Refrain from administering any form of antimicrobial therapy. Seek advice from Department of Genito-Urinary medicine.

4.7.5 Epididymo-orchitis

**Age Less Than 35 Years**

**First Line:** Ceftriaxone 500mg im or iv single dose **plus doxycycline** 100mg po every 12 hours

Duration: 14 days

**Second Line**
(Beta-lactam allergy):
Contact Consultant Microbiologist
Age Greater Than 35 Years Or Where STI Not Suspected

First Line: Ciprofloxacin 500mg po every 12 hours  
Duration: 10 days

4.8 Blood Stream Infections

4.8.1 INITIAL Management Of Infective Endocarditis (Pending Blood Culture Results)  
(BSAC 2012)

Ensure multiple blood cultures have been taken and contact Microbiology

Native Valve  
Indolent presentation

Native Valve  
Acute/severe presentation  
Or Penicillin Allergic

Native Valve  
Risk Factors for Multi-resistant Gram Negatives  
(VERY RARE)

Prosthetic Valve or intracardiac prosthesis

<table>
<thead>
<tr>
<th>Category</th>
<th>Antimicrobial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native Valve Indolent</td>
<td>Amoxicillin 2g iv every 4 hours</td>
</tr>
<tr>
<td>Native Valve Acute/severe</td>
<td>*Vancomycin iv (dose as per 3.4.2.1) PLUS *Gentamicin 1mg/kg IBW iv every 12 hours</td>
</tr>
<tr>
<td>Penicillin Allergic</td>
<td>*Vancomycin iv (dose as per 3.4.2.1) PLUS *Gentamicin 1mg/kg IBW iv every 12 hours</td>
</tr>
<tr>
<td>Risk Factors for Multi-resistant Gram Negatives</td>
<td>*Vancomycin iv (dose as per 3.4.2.1) PLUS Meropenem 2g iv every 8 hours</td>
</tr>
<tr>
<td>Prosthetic Valve or intracardiac prothesis</td>
<td>*Vancomycin iv (dose as per 3.4.2.1) PLUS *Gentamicin 1mg/kg IBW iv every 12 hours PLUS *Rifampicin 600mg iv or po every 12 hours</td>
</tr>
</tbody>
</table>

* Dose may have to adjusted according to levels or hepatic/renal function. See Section 3.4

Therapy to be adjusted, in accordance with national guidelines, once causative organism identified.  
(IBW = Ideal Body Weight)

4.8.2 Septicaemia/Sepsis Syndrome

Further treatment of septicaemia is based on site of probable origin of the infection.

Specimens: Blood culture. It is essential to collect at least 1 set before starting antibiotics. If clinical circumstances permit, a further 2 sets may be taken, by separate venepuncture, during a 2-4 hour period.

Duration: Appropriate broad spectrum antimicrobials should be commenced within 1 hour of presentation. In all cases intravenous antibiotics should be given for not less than 2 days and should continue for at least 24 hours after clinical recovery. If no clinical response after 48 hours, contact Consultant Microbiologist.
4.8.3  Sepsis syndrome, Of Unknown Origin

First Line:  Piperacillin/tazobactam 4.5g iv every 8 hours +/- gentamicin stat (7mg/kg ideal body weight)

Second Line
(Minor penicillin rash):
Cefuroxime 1.5g iv every 8 hours plus metronidazole 500mg iv every 8 hours plus gentamicin (7mg/kg ideal body weight, frequency according to Hartford Nomogram) see section 3.4.3.2 for exclusions.

Third Line
(Severe Beta-lactam allergy):
Vancomycin iv (dose as per 3.4.2.1) plus metronidazole 500mg iv every 8 hours plus ciprofloxacin 500mg po every 12 hours (400mg iv every 12 hours)

Note: where source is known, refer to recommendations of Sepsis Poster (see Annex 9)

4.8.4  Neutropenic Sepsis

Initial therapy to be reviewed within 48 hours.

First Line:  Stat gentamicin 7mg/kg ideal body weight plus piperacillin/tazobactam 4.5g iv every 6 hours +/- continue gentamicin 7mg/kg ideal body weight, (frequency according to Hartford Nomogram, see section 3.4.3.2 for exclusions) depending on clinical response.

Second Line
(Minor penicillin rash):
Meropenem 1g iv every 8 hours (2g every 8 hours in severe sepsis) +/- gentamicin 7mg/kg ideal body weight, (frequency according to Hartford Nomogram, see section 3.4.3.2 for exclusions) depending on clinical response.

Third Line
(Severe beta-lactam allergy/MRSA risk):
Stat gentamicin 7mg/kg plus ciprofloxacin 400mg iv every 8 hours (or 750mg po every 12 hours) plus vancomycin iv (dose as per 3.4.2.1) plus metronidazole 500mg iv 8 hourly

Refer to local policy for management of adult patients with Neutropenic sepsis. Note: Piperacillin/tazobactam alone may be unreliable in up to 12% of infections due to the prevailing sensitivity patterns of local Gram-negative rods.

4.8.5  Septicaemia – MRSA Suspected

First Line:  Vancomycin iv (dose as per 3.4.2.1) plus gentamicin 7mg/kg stat iv

Second Line:  Daptomycin 6mg/kg iv od plus gentamicin 7mg/kg stat iv

Third Line:  Consult Consultant Microbiologist

4.8.6  Septicaemia – ESBL Risk

First Line:  Temocillin 2g iv every 12 hours

Second Line
(Minor penicillin rash):
Ertapenem 1g iv od

Third Line
(Severe Beta-lactam allergy/MRSA risk):
Consult Consultant Microbiologist
4.8.7 Infections Associated With In-dwelling Intravascular Cannulae

First Line: Remove or change the line if practicable
Second Line: Consider need for line lock

If **indolent presentation** (probably due to Gram positive organisms): **vancomycin** iv (dose as per 3.4.2.1) and consider need for line lock

If **acute presentation** (probably due to Gram negative organisms): **gentamicin** 7mg/kg dose frequency according to Hartford Nomogram (see section 3.4.3.2 for exclusions)

Third Line Consult Consultant Microbiologist

4.8.8 Sepsis syndrome associated with yeasts/fungaemia in non-neutropenic patient

First Line: Intravenous **echinocandin*** for 14 days.

* Echinocandins are high cost drugs usually governed by supra-regional contracts. As such the compound in stock may vary from time to time. The appropriate doses of each compound currently on formulary is as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Starting Dose</th>
<th>Subsequent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anidulafungin</td>
<td>200mg od</td>
<td>100mg od</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>70mg od</td>
<td>50mg od (up to 80kg body weight)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70mg od (&gt;80kg body weight)</td>
</tr>
</tbody>
</table>

Change all in-dwelling lines. **DO NOT RAILROAD.** Perform fundoscopy to check for retinal deposits. Echocardiogram strongly advised. Repeat blood cultures at the end of therapy.

4.9 Ophthalmic infections

4.9.1 Conjunctivitis In Persons Who Do NOT Wear Contact Lenses

**NB:** Do not use steroid-containing eye medications. If no response after 3 days treatment, seek advice from Ophthalmologists.

First Line: **Chloramphenicol** 0.5% drops: apply 1 drop every 3-4 hours, topical.

Second Line: **Fusidic acid** 1% gel: apply 1 drop every 12 hours, topical.

Third Line: **Ofloxacin** 0.3% drops: apply 1 drop every 3-4 hours, topical.

Duration: Until 48 hours after clinical resolution – up to 7 days.

4.9.2 Conjunctivitis In Persons Who Wear Contact Lenses

**NB:** Do not use steroid-containing eye medications. If no response after 3 days treatment, seek advice from Ophthalmologists.
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications

First Line: **Gentamicin** 0.3% drops: apply 1 drop every 3-4 hours, topical.

Second Line: **Ofloxacin** 0.3% drops: apply 1 drop every 3-4 hours, topical.

Duration: Until 48 hours after clinical resolution – up to 7 days.

4.9.3 Conjunctivitis, Chlamydial

First Line: Clarithromycin 500mg po every 12 hours

Duration: 10 days

4.9.4 Conjunctivitis, Post-traumatic

Seek advice from Ophthalmologists before commencing treatment.

The following agents are available for prescription by Ophthalmology Registrars and above ONLY:

- **Cefuroxime** 5% eye drops
- **Gentamicin** 1.4% eye drops

4.9.5 Facial Cellulitis

First Line: Co-amoxiclav 1.2g iv every 8 hours. Consider the need for additional amoxicillin. See Section 3.2.

Second Line (minor penicillin rash): Cefuroxime 1.5g iv every 8 hours.

Third Line

(Severe beta-lactam allergy/MRSA risk) Vancomycin iv (dose as per section 3.4.2.1) PLUS clindamycin 450mg po every 6 hours

Duration: 7 – 10 days

4.9.6 Periorbital (pre-septal) and Orbital (post-septal) Cellulitis

Distinguish between pre-septal and post-septal cellulitis. If unclear, then initial management should be as post-septal cellulitis. Urgent ENT and ophthalmology review is required.

4.9.6.1 Periorbital cellulitis (>12 years)

Inpatient treatment

First Line: Piperacillin/tazobactam 4.5g iv every 8 hours

Second Line (minor penicillin rash): Cefuroxime 1.5g iv every 8 hours

Third Line (Severe beta-lactam allergy) Ciprofloxacin 750mg po every 12 hours plus clindamycin 450mg po every 6 hours

If MRSA is suspected add Vancomycin iv (dose as per 3.4.2.1)

Duration: 7 – 10 days.

Once clinical improvement is noted switch to oral.
Outpatient treatment:

First Line: Co-amoxiclav 625mg every 8 hours and amoxicillin 500mg every 8 hours

Second Line (Severe beta-lactam allergy/MRSA risk) Ciprofloxacin 750mg po every 12 hours plus clindamycin 450mg po every 6 hours

Duration: 7 – 10 days.

4.9.6.2 Orbital (post-septal) cellulitis

Urgent ENT and ophthalmology review is required.

First Line: Meropenem 2g iv every 8 hours

Second Line (Severe beta-lactam allergy) Ciprofloxacin 750mg po every 12 hours plus clindamycin 450mg po every 6 hours

If MRSA is suspected add Vancomycin iv (dose as per 3.4.2.1)

Duration: 14 - 21 days (longer is there is evidence of osteomyelitis)

4.9.7 Erysipelas (Facial)

First Line: Flucloxacillin 2g iv every 6 hours

Duration: 5 days (Review daily with view to early oral switch.)

Second Line (Beta-lactam allergy): Clindamycin 450mg po every 6 hours

Duration: 5 days

4.9.8 Specialist Ophthalmological Problems including Endophthalmitis

Endophthalmitis (Ophthalmic Emergency)

Seek advice from Ophthalmologists before commencing treatment.

The following compounds are available for intravitreal use:

- Vancomycin From Moorfields Formulary 2006, 1mg in 0.1ml (up to 2mg)
- Amikacin From Moorfields Formulary 2006, 0.4mg in 0.1ml
- Ceftazidime From Moorfields Formulary 2006, 2mg in 0.1ml

Other conditions such as the following should be referred to ophthalmology before commencing treatment.

- Corneal Ulcers
- Acanthamoebic Keratitis
- Fungal Keratitis
- Ocular Toxoplasmosis
4.10 Bone & Joint Infections

Specimens: aspirate all discharging pus or synovial fluid and collect blood for culture.

4.10.1 Arthritis, Septic

Referral to Orthopaedics is recommended in all cases

First Line: Flucloxacillin 2g iv every 6 hours
Duration: Review after 14 days

Second Line (Beta-lactam allergy): Clindamycin 450mg po every 6 hours
Duration: Review after 14 days

Third Line: Contact Consultant Microbiologist

Note: Follow on oral therapy may be required for many weeks.

4.10.2 Osteomyelitis, Acute

Referral to Orthopaedics is recommended in all cases

First Line: Flucloxacillin 2g iv every 6 hours

Discuss addition of second agent with Microbiologist once diagnosis is confirmed

Second Line (Beta-lactam allergy): Contact Consultant Microbiologist

4.10.3 Osteomyelitis, Chronic (Following Surgery Or Trauma)

NB: Endeavour to isolate causative agent before attempting antimicrobial therapy. Treat according to infecting organism(s).

4.10.4 Osteomyelitis, Secondary To Diabetic Ulcers

Refer to Diabetic Team, MDT required

4.10.5 Open Fracture (See also 5.4.8)

First Line: Flucloxacillin 2g loading thereafter 1g iv every 6 hours and metronidazole 500mg iv every 8 hours; add gentamicin 160mg iv stat if “soil” present

Second Line: Cefuroxime 1.5g iv every 8 hours and metronidazole 500mg iv every 8 hours; add gentamicin 160mg iv single dose if “soil” present

Third Line: Teicoplanin 200 to 800mg iv (see table in 5.4) daily and metronidazole 500mg iv every 8 hours; add gentamicin 160mg iv single dose if “soil” present

Duration: Continue until soft tissue closure has been achieved or for 72 hours whichever occurs first.
4.10.6 Discitis

First Line: Ciprofloxacin 500mg po every 8 hours (or 400mg iv every 8 hours) plus rifampicin 600mg po every 12 hours (The same dose may be given iv initially if required.)

Duration: At least 4 weeks
5 Prophylaxis

5.1 Benefits & Risks of Antibiotic Prophylaxis

The final decision regarding the benefits and risks of prophylaxis for an individual patient will depend on:

- The patient's risk of SSI
- The potential severity of the consequences of SSI
- The effectiveness of prophylaxis in that operation
- The consequences of prophylaxis for that patient (for example, increased risk of colitis.)

Benefits Of Prophylaxis

In many ways, the value of surgical antibiotic prophylaxis in terms of the incidence of SSI after elective surgery is related to the severity of the consequences of SSI. For example, in the presence of an anastomosis of the colon, prophylaxis reduces postoperative mortality. In total hip replacement surgery prophylaxis reduces long-term postoperative morbidity. For most operations, however, prophylaxis only decreases short-term morbidity.

Surgical site infection increases the length of hospital stay. The additional length of stay is dependent on the type of surgery. Prophylaxis has the potential to shorten hospital stay. There is little direct evidence that it does so as few randomised trials have included hospital length of stay as an outcome measure. There is evidence to indicate that prevention of wound infection is associated with faster return to normal activity after discharge from hospital.

Risks Of Prophylaxis

One of the aims of rationalising surgical antibiotic prophylaxis is to reduce the inappropriate use of antibiotics thus minimising the consequences of misuse.

Antibiotic-Associated Diarrhoea

No evidence was identified on how to reduce the incidence of antibiotic-associated diarrhoea (AAD) in patients receiving prophylactic antibiotics.

A single randomised controlled trial (RCT) suggested that the yeast Saccharomyces boulardii, in addition to standard antibiotics, reduced the risk of antibiotic-associated diarrhoea in children from 23% to 8% compared to placebo (number needed to treat; NNT -8). The incidence of Clostridium difficile was also reduced. A meta-analysis of the use of S. boulardii for preventing antibiotic-associated diarrhoea in adults was inconclusive, as the studies were heterogeneous and used different definitions of antibiotic-associated diarrhoea.

Treatment with S. boulardii may increase the risk of fungaemia especially in immunocompromised patients. More research is required before a recommendation on the use of S. boulardii can be made.

A study of yoghurt to prevent AAD in adults showed that yoghurt twice daily for 8 days whilst receiving intravenous antibiotics reduced the incidence of AAD from 23 out of 97 to 13 out of 105 patients (p-0.04, NNT-9). It is unclear whether this treatment would be useful during a short course of prophylactic antibiotic. The level of active Lactobacillus in the yoghurt is also difficult to assess.

Clostridium difficile-Associated Diarrhoea

Five per cent of healthy adults are reported to be carrying Clostridium difficile (C diff) on arrival at hospital. Patients who have been treated with broad spectrum antibiotics are at greatest risk of C diff associated disease. The risk of contracting C diff is raised for patients who:

- Are elderly
- Have a serious underlying illness that compromises their immune system
- Have a prolonged stay in healthcare settings
• Have recently had gastrointestinal surgery
• Are in hospital when there is an outbreak

The number of death certificates in England and Wales mentioning C diff associated diarrhoea (CDAD) has been on the increase since 1999. In 2005, 3,807 death certificates mentioned C diff, a 69% increase from 2004. C diff was the underlying cause of death in a similar proportion of cases each year (around 5%).

The prevalence of C diff associated diarrhoea is related to total antibiotic usage and, in particular, to the use of third generation cefalosporins.

In epidemiological studies of C diff colitis, surgical antibiotic prophylaxis is the single most common indication for use of antibiotics, and even single dose prophylaxis increases the risk of carriage of C diff.

It is not clear how many patients have C diff induced diarrhoea following antibiotic prophylaxis. No evidence was identified on how to prevent or reduce C diff associated diarrhoea in patients requiring prophylactic antibiotic treatment.

A meta-analysis of inconsistent and poor quality studies was unable to draw a conclusion about the efficacy of antibiotic treatment for C diff associated diarrhoea, nor about the antibiotic of choice for treating C diff associated diarrhoea.

Antibiotic Resistance

Rates of antibiotic resistance are increasing in all hospitals. The prevalence of antibiotic resistance in any population is related to the proportion of the population that receives antibiotics, and the total antibiotic exposure.

Increased antibiotic use leads to more resistance as demonstrated by a variety of large and small scale studies.

Three uncontrolled observational studies showed that when antibiotics were given for surgical prophylaxis there was an increased risk of the patients treated acquiring antibiotic resistant strains following treatment. Two trials of patient exposure to a single dose of either ciprofloxacin or vancomycin showed an absolute increase in the number of people with resistant organisms following treatment compared to pre-treatment (4 versus 8%). Prolonged prophylaxis (>48 hours) in coronary artery bypass graft (CABG) surgery was associated with an increased risk of acquired antibiotic resistance (odds ratio; OR of 1.6). No information was available about patient selection and only 41% of patients had cultures taken.

A small study comparing short term (24 hour) with longer term (5 day) prophylaxis following excision of head and neck lesions found significantly fewer patients with wounds infected by MRSA in the short term group (4/33 compared with 13/31).

The duration of prophylactic antibiotic therapy should be single dose except in special circumstances (for example prolonged surgery, major blood loss).

Multi-resistance Carriage

No evidence was identified to show whether carriage of multi-resistant organisms is associated with more frequent postoperative surgical site infection than carriage of sensitive strains.

In medical patients, carriage of MRSA is strongly predictive of subsequent MRSA infection in the short or long-term.

Extrapolation of this data to surgical patients suggests that MRSA carriage may be a risk factor for SSI. Preoperative care and choice of prophylactic antibiotic may need to be modified where patients are colonised with MRSA.

Carriage of multi-resistant organisms should be recognised as a potential risk factor for surgical site infection during high-risk operations (for example, orthopaedic implant, heart valve, vascular graft or shunt or CABG).
For patients with suspected multi-resistance carriage undergoing high risk operations preoperative care should include:

- Screening for relevant organisms
- Changing the antibiotic of choice for prophylaxis

### 5.2 Medical Prophylaxis

#### 5.2.1 Endocarditis Prophylaxis

In keeping with current NICE recommendations (Prophylaxis against infective endocarditis, NICE Clinical guideline 64, March 2008), routine antibiotic prophylaxis against infective endocarditis is **NO LONGER ADVISED.**

#### Cardiac Conditions Associated With A High Risk Of Endocarditis

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic cardiac valves including bio prosthetic and homograft valves.</td>
</tr>
<tr>
<td>Previous bacterial endocarditis.</td>
</tr>
<tr>
<td>Complex cyanotic heart disease (e.g. single ventricle states, transposition of the great arteries, Tetralogy of Fallot).</td>
</tr>
<tr>
<td>Surgically constructed systemic pulmonary shunts or conduits.</td>
</tr>
<tr>
<td>Acquired valvular heart disease with stenosis or regurgitation</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
</tr>
</tbody>
</table>

However, patients with high risk cardiac conditions (see box above) who are undergoing a gastrointestinal or genitourinary procedure where there is a known infection, use the following prophylactic regimen RATHER than that listed in section 5.3 below unless the infecting organism is known whereupon appropriately targeted antibiotics should be used instead.

#### Antibiotics For Patients Not Allergic To Penicillin

<table>
<thead>
<tr>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
</tr>
<tr>
<td>A single iv dose of 1g (children &lt;5 years of age: 250mg; ≥5 &lt;10 years of age: 500mg) given just before the procedure or at induction of anaesthesia</td>
</tr>
<tr>
<td>PLUS gentamicin 1.5mg/kg iv (max.160mg) (plus add metronidazole if it is normally part of the routine prophylaxis for the procedure being undertaken)</td>
</tr>
</tbody>
</table>

#### Antibiotics For Patients Allergic To Penicillin

<table>
<thead>
<tr>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teicoplanin</td>
</tr>
<tr>
<td>A single dose of 200mg – 800mg (see table in section 5.4) iv (children: &lt; 14 years 6mg/kg) given just before the procedure or at induction of anaesthesia</td>
</tr>
<tr>
<td>PLUS gentamicin 1.5mg/kg iv (max. 160mg) (plus add Metronidazole if it is normally part of the routine prophylaxis for the procedure being undertaken)</td>
</tr>
</tbody>
</table>

**NB:** AVOID Cefalosporins

If in doubt, contact the Consultant Microbiologist.

#### 5.2.2 Prophylaxis of Meningitis

Prophylaxis of contact of meningitis cases lies within the remit of the Consultant in Communicable Disease Control. The CCDC’s office will advise as to who requires prophylaxis and the appropriate agent(s) to use. However, for further advice, see [http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947389261](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947389261)
5.3 **Endoscopic, Radiological & Cardiological Procedures**

5.3.1 **ERCP, Biliary Stenting or PEG Insertion**

*First Line:* Gentamicin 160mg

5.3.2 **Long Line Insertion**

Antibiotic prophylaxis is not recommended.

5.3.3 **Uncomplicated Insertion of Cardiac Pacemaker or Similar Device**

*First Line*  
Teicoplanin 200 - 800mg iv (see table in 5.4)

*Second Line*  
Contact Consultant Microbiologist

5.4 **Surgical Prophylaxis**

When surgical prophylaxis is prescribed, an explicit entry about this clinical indication must be documented in the notes and prescribed as “surgical prophylaxis” on the ‘once only’ section of the prescription chart.

As a general rule of thumb, prophylaxis for surgical procedures should be a single dose, pre-operatively on induction of anaesthesia or at most within 60 minutes prior to incision; (unless otherwise specified in these guidelines).

Prophylaxis should not continue beyond 24 hours post operation in any event.

Antimicrobials continuing beyond 24 hours post operation are no longer prophylaxis and should be considered as treatment for early or established sepsis.

- The recommended antibiotic doses are intended for adult patients with normal renal and liver function.
- The antibiotic(s) should be administered during induction of anaesthesia ensuring that surgery starts within 30 minutes of this time.
- Further doses in addition to those listed are at the discretion of the Consultant.
- If the operation lasts more than 4 hours or the patient has greater than 1500 ml blood loss, an additional intro-operative dose may need to be given.

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40kg</td>
<td>200mg</td>
</tr>
<tr>
<td>40 – 80kg</td>
<td>400mg</td>
</tr>
<tr>
<td>&gt;80kg</td>
<td>800mg</td>
</tr>
</tbody>
</table>
5.4.1 Head & Neck Surgery

- **Head & Neck Surgery (Clean, Benign)**
  
  Antibiotic prophylaxis is not recommended.

- **Head & Neck Surgery (Contaminated/Clean-contaminated)**
  
  First Line: Co-amoxiclav 1.2g iv
  Second Line (Minor penicillin rash): Cefuroxime 1.5g iv plus metronidazole 500mg iv
  Third Line:
  (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv plus metronidazole 500mg iv

- **Head & Neck Surgery (Clean, Malignant, Neck Dissection)**
  
  Antibiotic prophylaxis should be considered.
  
  First Line: Co-amoxiclav 1.2g iv
  Second Line (Minor penicillin rash): Cefuroxime 1.5g iv plus metronidazole 500mg iv
  Third Line:
  (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv plus metronidazole 500mg iv

5.4.2 Maxillo Facial Surgery/ENT

- **Dentoalveolar Surgery – Simple Extraction**
  
  Antibiotic prophylaxis not recommended.

- **Dentoalveolar Surgery – Surgical Removal Of Teeth**
  
  Antibiotic prophylaxis not recommended.

- **Dentoalveolar Surgery – Wisdom Teeth Removal With Extensive Bone Removal**
  
  First Line: Co-amoxiclav 1.2g iv
  Second Line (Minor penicillin rash): Cefuroxime 1.5g iv plus metronidazole 500mg iv
  Third Line:
  (Severe beta-lactam allergy): Metronidazole 500mg

- **Dentoalveolar Surgery - Apical Surgery**
  
  Antibiotic prophylaxis not recommended.

- **Dentoalveolar Surgery – Intra-oral Bone Grafting**
  
  First Line: Co-amoxiclav 1.2g iv
  Second Line (Minor penicillin rash): Cefuroxime 1.5g iv plus metronidazole 500mg iv
  Third Line:
  (Severe beta-lactam allergy): Metronidazole 500mg
- **Dentoalveolar Surgery – Osseointegrated Implants**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv plus metronidazole 500mg
  
  **Third Line (Severe beta-lactam allergy):** Metronidazole 500mg

- **Facial Surgery – Open Reduction & Internal Fixation Of Compound Mandibular Fractures**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv plus metronidazole 500mg
  
  **Third Line (Severe beta-lactam allergy):** Clindamycin 600mg iv

- **Facial Surgery – Intraoral Bone Grafting Procedures**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv plus metronidazole 500mg
  
  **Third Line (Severe beta-lactam allergy):** Clindamycin 600mg iv

- **Routine Nose, Sinus & Endoscopic Sinus Surgery:** Antibiotic prophylaxis not recommended.

- **Complex Septorhinoplasty Including Grafts**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv plus metronidazole 500mg
  
  **Third Line (Severe beta-lactam allergy):** Gentamicin 160mg plus clindamycin 600mg iv

- **Tonsillectomy And/Or Adenoidectomy**
  
  Antibiotic prophylaxis not recommended.

### 5.4.3 Breast Surgery

- **Breast Surgery – Breast Cancer Surgery**
  
  **First Line:** Flucloxacillin 1g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/PREVIOUS MRSA Positive):** Teicoplanin 200 - 800mg iv (see table in 5.4)
**Breast Surgery – Breast Reshaping Procedures**

- **First Line:** Flucloxacillin 1g iv
- **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv
- **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Teicoplanin 200 - 800mg iv (see table in 5.4)

**Breast Surgery – Breast Surgery With Prosthetic Implant**

- **First Line:** Flucloxacillin 1g iv every 6 hours for 24 hours
- **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv every 8 hours for 24 hours
- **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Teicoplanin 200 - 800mg iv (see table in 5.4) every 12 hours for 24 hours

**Breast Surgery – Breast Surgery Reconstruction**

- **First Line:** Flucloxacillin 1g iv
- **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv
- **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Teicoplanin 200 - 800mg iv (see table in 5.4)

### 5.4.4 Gastrointestinal Surgery

**Upper Gastrointestinal – Oesophageal Surgery**

- **First Line:** Gentamicin 160mg iv
- **Second Line (Minor penicillin rash):** Gentamicin 160mg iv
- **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv

**Upper Gastrointestinal – Stomach And Duodenal Surgery**

- **First Line:** Gentamicin 160mg iv
- **Second Line (Minor penicillin rash):** Gentamicin 160mg iv
- **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv
- **Upper Gastrointestinal – Gastric Bypass Surgery**
  
  First Line: **Gentamicin 160mg iv**
  
  Second Line (Minor penicillin rash): **Gentamicin 160mg iv**
  
  Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv**

- **Upper Gastrointestinal – Small Intestine Surgery**
  
  First Line: **Gentamicin 160mg iv**
  
  Second Line (Minor penicillin rash): **Gentamicin 160mg iv**
  
  Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv**

- **Hepatobiliary – Bile Duct Surgery**
  
  First Line: **Co-amoxiclav 1.2g iv**
  
  Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv and metronidazole 500mg iv**

- **Hepatobiliary – Pancreatic Surgery**
  
  First Line: **Co-amoxiclav 1.2g iv**
  
  Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv and metronidazole 500mg iv**

- **Hepatobiliary – Liver Surgery**
  
  First Line: **Co-amoxiclav 1.2g iv**
  
  Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv and metronidazole 500mg iv**

- **Hepatobiliary – Cholecystectomy Open**
  
  First Line: **Co-amoxiclav 1.2g iv**
  
  Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive): **Gentamicin 160mg iv and metronidazole 500mg iv**
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications

- **Hepatobiliary – Cholecystectomy Laparoscopic** (high risk patients only e.g. if intra-operative cholangiogram, bile spillage, conversion to laparotomy, acute cholecystitis/pancreatitis, jaundice, pregnancy, immunosuppression, insertion of prosthetic devices)
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line**
  (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Gentamicin 160mg iv and metronidazole 500mg iv

- **Lower Gastrointestinal – Appendicectomy**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line**
  (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Gentamicin 160mg iv and metronidazole 500mg iv
  
  **Third Line**
  Contact Consultant Microbiologist

- **Lower Gastrointestinal – Colorectal Surgery**
  
  **First Line:** Co-amoxiclav 1.2g iv +/- metronidazole 500mg iv
  
  **Second Line** (Minor penicillin rash):
  Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line**
  (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Gentamicin 160mg iv and metronidazole 500mg iv

- **Lower Gastrointestinal – Flap Surgery For Pilonidal Sinus**
  
  **First Line:** Co-amoxiclav 1.2g iv every 8 hours for 24 hours
  
  **Second Line** (Minor penicillin rash):
  Cefuroxime 750mg iv every 8 hours and metronidazole 500mg iv every 8 hours for 24 hours
  
  **Third Line**
  (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Gentamicin 160mg stat plus teicoplanin 400mg every 12 hours and metronidazole 500mg every 8 hours for 24 hours

- **Lower Gastrointestinal – Laparoscopy / Laparotomy - Without Mucosal Breach**
  
  **First Line:** None

- **Lower Gastrointestinal – Stapled Haemorrhoidectomy**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line** (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
  Gentamicin 160mg iv and metronidazole 500mg iv
  
  **Third Line**
  Contact Consultant Microbiologist
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications

- **Hernia Repair – Inguinal, Femoral Or Incisional, With Or Without Mesh.**
  Antibiotic prophylaxis not recommended.

- **Abdomen – Diagnostic Endoscopic Procedures**
  
  *First Line: None*

- **Abdomen – Therapeutic Endoscopic Procedures***
  
  *First Line:*
  
  Gentamicin 160mg iv

  *Second Line (Minor penicillin rash):*
  
  Gentamicin 160mg iv

  *Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):*
  
  Gentamicin 160mg iv

* This category includes operations such as ERCP, PEG insertion and surgical high risk surgery with mesh insertion, eg gastric banding, etc.

- **Spleen – Elective Splenectomy**
  Consider in immunosuppressed patients

  *First Line:*
  
  Flucloxacillin 1g iv

  *Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):*
  
  Teicoplanin 200 - 800mg iv (see table in 5.4)

5.4.5 Vascular Surgery

- **Vascular Surgery – Amputation With Pre-existing Infection And / Or Diabetes etc**
  
  *First Line:*
  
  Co amoxiclav 1.2g iv

  *Second Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):*
  
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv plus metronidazole 500mg iv

- **Vascular Surgery – Amputation Following Major Trauma**
  
  *First Line:*
  
  Co amoxiclav 1.2g iv followed by metronidazole 400mg po or 500mg iv every 8 hours for 5 days

  *Second Line:*
  
  Cefuroxime 750mg iv plus metronidazole 500mg iv followed by metronidazole 400mg po or 500mg iv every 8 hours for 5 days

  *Third Line (Beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):*
  
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv stat plus metronidazole 500mg iv followed by metronidazole 400mg po or 500mg iv every 8 hours for 5 days
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications.
- **Abdominal Approach Surgery – Laparotomy / Laparoscopy (Without Mucosa Breach)**
  Antibiotics not indicated.

- **Abdominal Approach Surgery – Total Abdominal Hysterectomy**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv and clindamycin 600mg iv

- **Abdominal Approach Surgery – Colorectal / Ileal resection**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv and metronidazole 500mg iv

- **Vaginal Approach Surgery – Vaginal Hysterectomy**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv and clindamycin 600mg iv

- **Vaginal Approach Surgery – Anterior Repair**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv and clindamycin 600mg iv

- **Vaginal Approach Surgery – Posterior Repair**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv and metronidazole 500mg iv
  
  **Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):** Gentamicin 160mg iv and clindamycin 600mg iv
Vaginal Approach Surgery – Tension-free Vaginal Tape Obdurator

First Line: Co-amoxiclav 1.2g iv
Second Line (Minor penicillin rash): Cefuroxime 750mg iv and metronidazole 500mg iv
Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
Gentamicin 160mg iv and clindamycin 600mg iv

Vaginal Approach Surgery – Surgical Termination Of Pregnancy

First Line: Azithromycin 1g po and metronidazole 1g pr

Vaginal Approach Surgery – Evacuation Of Incomplete Miscarriage

First Line: None

Vaginal Approach Surgery – Intra-uterine Contraceptive Device Insertion

First Line: None

5.4.7 Ophthalmic Surgery

Cataract Surgery

Topical antimicrobials only in line with local departmental protocols.

5.4.8 Orthopaedic Surgery

Large Joint Arthroplasty

First Line: Gentamicin 160mg iv + flucloxacillin 2g iv followed by 3 further doses of flucloxacillin 1g iv every 6 hours
Second Line (Minor penicillin rash): Cefuroxime 1.5g iv; followed by 2 further doses of cefuroxime 750mg iv every 8 hours if surgeon requests
Third Line (Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
Teicoplanin 200 - 800mg iv (see table in 5.4) and gentamicin 160mg iv. If surgeon requires further doses, discuss with Microbiologist

Small Joint/Day Case Arthroplasty

Follow locally agreed guidelines if at variance to large joint arthroplasty above.
Open Fracture (See also 4.10.5)

First Line:
- **Flucloxacillin** 2g loading thereafter 1g iv every 6 hours and **metronidazole** 500mg iv every 8 hours; add **gentamicin** 160mg iv stat if “soil” present

Second Line:
(Minor penicillin rash):
- **Cefuroxime** 1.5g iv every 8 hours and **metronidazole** 500mg iv every 8 hours; add **gentamicin** 160mg iv single dose if “soil” present

Third Line:
(Severe beta-lactam allergy/MRSA risk):
- **Teicoplanin** 200 to 800mg iv (see table in 5.4) daily and **metronidazole** 500mg iv every 8 hours; add **gentamicin** 160mg iv single dose if “soil” present

Duration
- Continue until soft tissue closure has been achieved or for 72 hours whichever occurs first.

Open Surgery For Closed Fracture

First Line:
- **Gentamicin** 160mg iv + **flucloxacillin** 2g iv

Second Line (Minor penicillin rash):
- **Cefuroxime** 1.5g iv

Third Line
(Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
- **Teicoplanin** 200 - 800mg iv (see table in 5.4) and **gentamicin** 160mg iv

Orthopaedic Surgery (Without Implant)

Antibiotic prophylaxis not recommended.

Hip Fracture (DHS)

First Line:
- **Gentamicin** 160mg iv + **flucloxacillin** 2g iv

Second Line (Minor penicillin rash):
- **Cefuroxime** 1.5g iv; followed by 2 further doses **cefuroxime** 750mg iv every 8 hours if surgeon requests

Third Line
(Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
- **Teicoplanin** 200 - 800mg iv (see table in 5.4) and **gentamicin** 160mg iv.
  - If surgeon requires further doses, discuss with Microbiologist

Amputation With Pre-existing Infection And / Or Diabetes etc

First Line:
- **Co-amoxiclav** 1.2g iv

Second Line (Minor penicillin rash):
- **Cefuroxime** 750mg iv and **metronidazole** 500mg iv

Third Line
(Severe beta-lactam allergy/MRSA risk/ PREVIOUS MRSA Positive):
- **Gentamicin** 160mg iv and **metronidazole** 500mg iv

BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS
Antibiotic Formulary Prescribing Advice Adult V7.1.docx
Printed copies are not controlled and are valid on date of printing only. This version was last printed: 15/12/2016

- **Amputation Following Major Trauma**
  
  **First Line:** Co-amoxiclav 1.2g iv every 8 hours for 5 days
  
  **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv plus metronidazole 500mg iv followed by metronidazole 500mg iv every 8 hours (400mg oral every 8 hours) for 5 days
  
  **Third Line**
  (Severe beta-lactam allergy/MRSA risk/
  PREVIOUS MRSA Positive):
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv and metronidazole 500mg iv followed by metronidazole 500mg iv every 8 hours (400mg oral every 8 hours) for 5 days

- **Spinal – Spinal Surgery**
  
  **First Line:** Gentamicin 160mg iv + flucloxacillin 2g iv followed by 3 further doses of flucloxacillin 1g iv every 6 hours
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv followed by 2 further doses of cefuroxime 750mg iv every 8 hours if metal work inserted
  
  **Third Line**
  (Severe beta-lactam allergy/MRSA risk/
  PREVIOUS MRSA Positive):
  Teicoplanin 200 - 800mg iv (see table in 5.4) plus gentamicin 160mg iv. If surgeon requires further doses, discuss with Microbiologist

- **Hand – Soft Tissue Of The Hand (Elective Procedure)**
  
  **First Line:** Co-amoxiclav 1.2g iv
  
  **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv
  
  **Third Line**
  (Severe beta-lactam allergy/MRSA risk/
  PREVIOUS MRSA Positive):
  Teicoplanin 200 - 800mg iv (see table in 5.4) and gentamicin 160mg iv

5.4.9 Urological Surgery

*In the presence of infected urine antibiotic prophylaxis should be targeted against the infecting organism*

- **Urethral or Suprapubic Catheterisation/Catheter removal**
  
  Antibiotic prophylaxis NOT routinely recommended.

- **Shockwave Lithotripsy (ESWL)**
  
  Prophylaxis not routinely indicated.

  If higher risk patient (past history of infection, ‘infection’ calculi, single kidney, immune suppression):

  **First Line:** Gentamicin 160mg iv
  
  **Second Line** Co-amoxiclav 1.2g iv
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications.

- **Percutaneous Nephrolithotomy/Endoscopic Ureteric Removal or Fragmentation of Stone**
  - **First Line:** Gentamicin 160mg iv
  - **Second Line:** Co-amoxiclav 1.2g iv

- **Percutaneous Insertion of Urostomy**
  - **First Line:** Gentamicin 160mg iv
  - **Second Line:** Co-amoxiclav 1.2g iv

- **Transurethral Resection of Bladder Tumours**
  Antibiotic prophylaxis NOT routinely recommended.

- **Radical Cystectomy**
  - **First Line:** Co-amoxiclav 1.2g iv
  - **Second Line (Minor penicillin rash):** Cefuroxime 750mg iv plus metronidazole 500mg iv
  - **Third Line (Severe beta-lactam allergy/MRSA risk/PREVIOUS MRSA Positive):** Gentamicin 160mg iv

- **Optical Urethrotomy**
  - **First Line:** Gentamicin 160mg iv

- **Radical Orchidectomy With Prosthesis**
  - **First Line:** Co-amoxiclav 1.2g iv
  - **Second Line (Minor penicillin rash):** Cefuroxime 1.5g iv
  - **Third Line (Severe beta-lactam allergy/MRSA risk/PREVIOUS MRSA Positive):** Gentamicin 160mg iv

- **Transurethral Resection of Prostate (TURP)**
  - **First Line:** Gentamicin 160mg iv
  - **Second Line:** Contact Consultant Microbiologist

In the presence of infected urine antibiotic prophylaxis should be targeted against the infecting organism.

- **Transrectal Or Transperineal Prostate Biopsy**
  - **First Line:** Ciprofloxacin 600mg iv (or 750mg po) plus metronidazole 500mg iv (or 400mg po)
  - **Second Line:** Meropenem 1g iv
  - **Third Line:** Contact Consultant Microbiologist
Radical Prostatectomy

First Line: Gentamicin 160mg iv

Nephrectomy

Antibiotic prophylaxis not routinely recommended.

Hydrocele repair

Antibiotic prophylaxis not routinely recommended.
6 De-escalation of IV to oral

6.1 Guidance on individual drugs

**Amoxicillin / co-amoxiclav:** Amoxicillin has good oral bioavailability (unlike ampicillin), the switch from iv to oral amoxicillin should take place as soon as a patient's clinical condition improves. Clavulanic acid also has good oral bioavailability so early iv to oral switch of co-amoxiclav should take place.

**Ciprofloxacin:** Oral bioavailability of ciprofloxacin is approximately 70%. A 200mg iv dose can be switched for a 250mg oral dose and the 400mg iv dose switched for a 500mg oral dose. Food delays the rate but not the extent of absorption. The oral formulation is significantly less expensive than the iv, so early switch to oral therapy is encouraged.

**Clarithromycin:** Clarithromycin should be given orally is possible to help avoid adverse reactions associated with the rate of iv infusion.

**Clindamycin:** Oral bioavailability of clindamycin is approximately 90%, so 300mg iv is approximately equivalent to 300mg orally. Food delays the rate but not the extent of absorption. The oral formulation is significantly less expensive than the iv, so early switch to oral therapy is encouraged.

**Flucloxacillin:** Oral bioavailability of flucloxacillin is approximately 80%. Consequently an oral dose of 500mg is approximately equivalent to 500mg iv. Absorption of oral flucloxacillin is reduced in the presence of food consequently doses should be administered half to one hour before meals.

**Fluconazole:** there is rapid absorption and widespread distribution after both oral and parenteral administration, with identical serum concentrations attained.

**Levofoxacin:** Rapid and almost complete absorption of levofoxacin occurs after oral administration producing an absolute bioavailability of nearly 100%. Peak concentrations are reached within 1 hour post administration. The oral formulation of levofoxacin is considerably less expensive than the iv one and so should be used where possible and an early switch from iv to oral levofoxacin is encouraged.

**Linezolid:** Linezolid has rapid and extensive absorption following oral dosing. The absolute bioavailability is complete (100%) and not significantly affected by food. Maximum plasma concentrations are reached within 2 hours of dosing and following oral administration steady state conditions are achieved by the 2nd day of dosing.

**Metronidazole:** Oral bioavailability is approximately 80-85% with a 500mg iv dose equivalent to 400mg oral. When the oral route is inappropriate the rectal route may be used. Effective blood concentrations are achieved within 5-12 hours.

**Moxifloxacin:** Rapid and almost complete absorption of moxifloxacin occurs after oral administration with an absolute bioavailability of approximately 91%. Peak concentrations are reached within 0.5 to 4 hours post administration. The oral formulation of moxifloxacin is considerably less expensive than iv moxifloxacin and so should be used where possible or an early switch from iv moxifloxacin to oral moxifloxacin is encouraged.

**Rifampicin:** Oral bioavailability is near 100%. However a 600mg oral dose gives a peak plasma concentration similar to a 3-hour 600mg iv infusion. Food delays the rate and extent of absorption so an oral dose should be taken at least 30 minutes before, or 2 hours after, food. The oral formulation is significantly less expensive than the iv, so early switch to oral therapy is encouraged.

**Vancomycin:** Vancomycin does not have significantly absorption following oral administration; consequently the iv formulation must always be used to treat systemic infection.
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Annex 1  **Splenectomy Patients**

**Guidelines For Prevention Of Infection In Patients With An Absent Or Dysfunctional Spleen**

Patients with splenic dysfunction or asplenia are at increased risk of overwhelming sepsis caused by encapsulated bacteria and other micro-organisms.

Although most infections occur within the first two years after splenectomy, up to one third may manifest at least five years later, and cases have occurred more than 20 years later. The risk of dying of serious infection is significant and almost certainly lifelong.

**Micro-organisms**

*Streptococcus pneumoniae* (pneumococcus) is the most common pathogen, and together with *H. influenzae* and *N. meningitides* (meningococcus) accounts for 70-90% of cases.

Other infections include *E. coli*, malaria, babesiosis, and *Capnocytophaga canimorsus* (associated with dog bites).

Preventative strategies are based on the education of staff and patients, appropriate immunisation schedules and antibiotic prophylaxis and treatment of proven or suspected infection.

**Immunisations – Timing**

In elective splenectomy cases administer at least 2 weeks pre-splenectomy if possible.

After emergency splenectomy, administer at hospital discharge or 2 weeks post splenectomy, whichever is sooner.

In patients with functional hyposplenism (e.g. due to immunosuppression), immunization should be undertaken no later than 2 weeks before or delayed for at least 3 months after immunosuppressive therapy, or until recovery of immunological function, where this can be assessed.

1. **Pneumococcal Immunisation**

Pneumococcal polyvalent (23-valent) unconjugated pneumococcal polysaccharide vaccine (PPV) is used for immunisation of persons older than 2 years of age, e.g. Pneumovax II®.

a. Check the level of pneumococcal antibodies 4 weeks post immunisation by sending a plain serum sample to Immunology, state the date of the immunisation on the form and specify that the patient is asplenic.

b. Responders should be re-vaccinated with PPV at 5 yearly intervals

However, antibody levels can fall rapidly in asplenic patients because a specific set of memory B cells normally resides in the spleen, so check pneumococcal antibody levels once a year. The protective level is not defined, but a precipitous fall should indicate that the Pneumovax booster should be given sooner than 5 years.

d. Serological non-responders to PPV may benefit from 2 doses of Pneumococcal Conjugate vaccine (e.g. Prevenar 13®), 2 months apart

2. **Haemophilus Influenzae Type B Vaccination**

Patients should receive one dose of a Hib-containing vaccine (e.g. Hib/MenC vaccine; i.e. Menitorix®), irrespective of their previous immunization status.
3. Meningococcal Immunisation

Patients should receive one dose of a Meningococcal C conjugate vaccine (e.g. Hib/MenC vaccine; i.e. Menitorix®), followed by a single dose of quadrivalent meningococcal conjugate vaccine that covers serotypes A, C, W135, Y (i.e. Menveo® or Nimenrix®) one month later, irrespective of their previous immunization status.

Travellers to endemic areas should also receive the quadrivalent MenACWY conjugate vaccine before travelling.

Please note there is a recently licensed 4CMenB vaccine (Bexsero®) to cover Group B meningococci. The need for, and the timing of, a booster dose of 4CMenB vaccine in at-risk individuals has not yet been determined.

Please refer to ‘The Green Book’ for currently available vaccines.

4. Influenza Vaccine

Due to the risk of secondary bacterial infection, give seasonal influenza vaccine annually.

<table>
<thead>
<tr>
<th>Vaccination Summary</th>
<th>Month 0</th>
<th>Month 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (regardless of vaccination history)</td>
<td>PPV (Pneumovax II®) Hib / MenC (Menitorix®) Influenza vaccine</td>
<td>MenACWY (Menveo® or Nimenrix®)</td>
</tr>
</tbody>
</table>

5. Post-immunisation Follow-up Testing

There is currently no routinely available assay for protective levels of pneumococcal antibodies – the current test gives a combined result for all antibodies against the 23 serotypes in the Pneumovax II® vaccine. However, a falling level may indicate declining immunological memory, and most immunologists favour antibody concentrations at least double the lower end of the normal range. In addition, some patients have an inability to respond to pure polysaccharide vaccines (specific polysaccharide antibody deficiency, SPAD). For this reason checking pneumococcal, Hib and Group C meningococcal polysaccharide antibody levels after the first vaccine and then only pneumococcal antibodies annually is recommended. The assay is invalid for patients who have received Prevenar®, as this is a protein-conjugate vaccine, however, poor antibody levels after Prevenar® may indicate a more serious immunodeficiency. In special circumstances, protective antibody levels against particular pneumococcal serotypes can be requested, and a measure of susceptibility define – please discuss all such cases with Immunology.

6. Antibiotic Prophylaxis

Most instances of serious infection are due to encapsulated bacteria, with pneumococcal disease being predominant. However, the role of life-long prophylaxis is less clear, with the emergence of penicillin resistant pneumococci. It is accepted that compliance may be a problem and that long-term antibiotic prophylaxis is controversial in the light of emerging antimicrobial resistance. The evidence for prophylactic antibiotics in adults, and outside the 2-year period after splenectomy is poor. Since there may be definite disadvantages of prophylactic antibiotics, the decision to use prophylactic antibiotics should be made on an individual basis with each patient, following discussion of the risk and disadvantages.

Factors associated with a high risk of invasive pneumococcal disease in hyposplenism or asplenia include; age less than 16 years or greater than 50 years, inadequate serological response to pneumococcal vaccination, a history of previous invasive pneumococcal disease and splenectomy for underlying haematological malignancy, particularly in the context of ongoing immunosuppression. Appropriate antibiotic prophylaxis should continue in these patients and for 2 years in the post-operative period following post-trauma splenectomy.

Patients not at high risk should be counselled regarding the risks and benefits of life-long antibiotics, so they are able to choose whether to continue or discontinue prophylaxis.
Fully immunised adults who choose not to continue prophylactic antibiotics should be supplied with an emergency supply of co-amoxiclav or clarithromycin if allergic to penicillin available at home. This should be used immediately if they develop symptoms of shivers, fever or malaise whilst immediate medical attention is sought. **This is the preferred option of the Path Links Microbiologists.**

**Otherwise, recommended continued prophylaxis is:**

Penicillin V 250mg every 12 hours orally  
Erythromycin 500mg every 12 hours (if penicillin allergic) orally

Patients developing symptoms and / or signs of infection, despite the above measures, must be given systemic antibiotics and admitted to hospital (see choices below).

7. **Education**

- Education of the patient about their life-long increased risk of overwhelming infection
- The need for malaria prophylaxis when travelling to affected areas is important
- They should be told to seek urgent medical attention if they develop fevers, shivers or feel unwell, or are bitten or scratched by an animal
- Possible occupational risk factors should be considered
- They should be issued with an alert card (available from Department of Health)

If acutely unwell and not penicillin allergic, prompt administration of benzylpenicillin or cefotaxime is recommended.
Annex 2  Influenza: Use Of Antivirals

Annex 3  **Antimicrobial Resistance And *Clostridium difficile* Strategy**

The increasing prevalence of antimicrobial resistant micro-organisms, especially those with multiple resistance, and *Clostridium difficile* - associated diarrhoea (CDAD), is causing international concern.

Antimicrobial resistance and CDAD make infections more difficult to treat. They may also increase the length and severity of illness, the period of infectiousness, adverse reactions, length of hospital admission and costs.

The emergence of resistance represents adaptive selection by micro-organisms which is to some extent an inevitable result of the therapeutic use of antimicrobial agents. This makes it imperative that measures are taken both to slow – or at least delay – the emergence of resistance, to the existing agents and to new ones as they come into use, and to limit its spread.

The overall aims of the strategy are:

In the face of the ability of micro-organisms resistant to antimicrobial agents to emerge and spread, the increasing prevalence of resistant strains and the dearth of new agents likely to be available for therapeutic use in the near future, and the rise in CDAD cases.

- to minimise the morbidity and mortality due to antimicrobial resistant infection and *Clostridium difficile*-associated disease;
- to maintain the effectiveness of antimicrobial agents in the treatment and prevention of microbial infections in patients.

The three key, inter-related, elements of the strategy to control antimicrobial resistance are:

**Surveillance:** to provide data on resistant organisms, *Clostridium difficile* and antimicrobial use;

**Prudent antimicrobial use:** to reduce the ‘pressure for resistance’ and proliferation of *Clostridium difficile* by reducing unnecessary and inappropriate exposure of micro-organisms to antimicrobial agents in clinical practice.

Additional caution is advised when prescribing antimicrobials in elderly patients, those who have had previous *Clostridium difficile* disease and those who are GDH-positive because they are at increased risk of *C. difficile* disease.

**NOTE:** There is no evidence that concomitant administration of metronidazole is protective.

**Infection Control:** to reduce the spread of infection in general and of antimicrobial resistant micro-organisms in particular.
Annex 4  Antibiotics in Pregnancy

Drug use in general in pregnancy is an extremely difficult issue for health care professionals. Antibiotics have the potential to cause harmful effects to the embryo or foetus at any time during the pregnancy. A balance between benefits to the mother and the associated risk to the foetus is required.

No drug is safe beyond all doubt in early pregnancy and so all drugs should be avoided if possible during the first trimester.

If an antibiotic is clearly necessary (following discussion with a senior member of the team) the least teratogenic drug should be selected, at the lowest effective dose and stop it as soon as possible where able.

The BNF identifies drugs which:

- May have harmful effects in pregnancy and indicates the trimester of risk
- Are not known to be harmful in pregnancy

For further information and support please contact the Medicines Information Department. Please remember to involve Obstetrics and Microbiology.

<table>
<thead>
<tr>
<th>NLAG</th>
<th>ULH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hours:</strong></td>
<td><strong>Monday to Friday 9am to 5pm</strong></td>
</tr>
<tr>
<td>8.45am to 5.15pm</td>
<td></td>
</tr>
<tr>
<td><strong>Phone:</strong></td>
<td><strong>01522 573802, if voicemail and your query is urgent bleep 3125</strong></td>
</tr>
<tr>
<td>01472 875273 or DPOWH 7560. Voicemail or if urgent, bleep 028</td>
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<td><strong>Email:</strong></td>
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</table>

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Grimsby
DN33 2BA

Medicines Information Service
Pharmacy Department
Lincoln County Hospital
Greetwell Road
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Annex 5  Continuous Vancomycin Infusion Guidelines in Critical Care

Adapted from Sheffield Teaching Hospitals Guidelines, V9 160512

Background

Vancomycin is bactericidal against many gram-positive organisms. The antimicrobial activity of vancomycin is dependent on the time that the serum concentration exceeds the minimum inhibitory concentration of the microorganism being treated¹. In critically ill patients with varying degrees of renal impairment, continuous vancomycin infusions have some advantages over intermittent dosing with regards to therapeutic drug management.

Indication

To treat infections in intensive care patients caused by aerobic and anaerobic Gram-positive bacteria including multi-resistant staphylococci. Its efficacy has been well documented in the treatment of endocarditis, osteomyelitis, pneumonia, sepsis and soft tissue infections.

Dose

Loading Dose²

All patients must receive a weight-related loading dose. This is based on their adjusted body weight calculated as follows:

\[
\text{Adjusted Body Weight} = \text{Ideal Body Weight} + 0.4 \times (\text{Total Body Weight} - \text{Ideal Body Weight})
\]

<table>
<thead>
<tr>
<th>Patient Adjusted Body Weight (kg)</th>
<th>Standard Loading Dose (mg)</th>
<th>Septic Shock/SIRS* Loading Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>750</td>
<td>1250</td>
</tr>
<tr>
<td>51 – 65</td>
<td>1000</td>
<td>1500</td>
</tr>
<tr>
<td>66 – 85</td>
<td>1250</td>
<td>2000</td>
</tr>
<tr>
<td>&gt;85</td>
<td>1500</td>
<td>2250</td>
</tr>
</tbody>
</table>

*Septic shock/SIRS loading dose is indicated for patients with:

- Septic shock (eg noradrenaline ≥0.2 microgram/kg/min)
- Polytrauma with Systemic Inflammatory Response (SIRS)
- Burns (affecting a significant proportion of body surface area with SIRS)

Maintenance Dose

The continuous maintenance infusion should follow straight after the loading dose and is dependent on the estimated renal function of the patient.

<table>
<thead>
<tr>
<th>Estimated Renal Clearance</th>
<th>Comments</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperdynamic with supranormal renal function</td>
<td>Eg trauma, burns patients &amp; increased Cl, UO and clearance</td>
<td>83mg/hr</td>
</tr>
<tr>
<td>Normal renal function</td>
<td>No evidence of renal dysfunction</td>
<td>63mg/hr</td>
</tr>
<tr>
<td>Moderate renal failure</td>
<td>SCR &gt;120 µmol/L + Urea &gt;8mmol/L + or UO &lt;800ml/24hr or UO &lt;200ml/6hr</td>
<td>42mg/hr</td>
</tr>
<tr>
<td>Severe renal failure</td>
<td>SCR &gt;240µmol/L + Urea &gt;16mmol/L + or UO &lt;400ml/24hr or UO &lt;100ml/6hr or measured CrCl &lt;20ml/minute</td>
<td>21mg/hr</td>
</tr>
<tr>
<td>CVVH or CVVHD or Intermittent CVVH</td>
<td>CVVH infusion rate ≥ 30ml/kg/hr</td>
<td>63mg/hr</td>
</tr>
</tbody>
</table>

Cl = Cardiac Index; UO = Urine Output; SCR = Serum Creatinine; CrCl = Creatinine Clearance
NB: When determining the dose, also consider whether renal impairment is acute or chronic. Other factors to take into account are measured creatinine clearance and small muscle mass.

Rate Adjustments when introducing or discontinuing Renal Replacement Therapy in patients with Acute Renal Failure (ARF) and already receiving vancomycin infusion

### Preparation

**Loading Dose**

Reconstitute each vancomycin 500mg vial in 10ml water for injection and then dilute as follows:

<table>
<thead>
<tr>
<th>Loading Dose</th>
<th>750mg</th>
<th>1000mg</th>
<th>1250mg</th>
<th>1500mg</th>
<th>2000mg</th>
<th>2250mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central line</td>
<td>100ml</td>
<td>100ml</td>
<td>100ml</td>
<td>100ml</td>
<td>250ml</td>
<td>250ml</td>
</tr>
<tr>
<td>Peripheral line</td>
<td>250ml</td>
<td>250ml</td>
<td>250ml</td>
<td>500ml</td>
<td>500ml</td>
<td>500ml</td>
</tr>
</tbody>
</table>

**Maintenance Continuous Infusion**

- **Central:** Use a docked bag of vancomycin 1000mg/100ml
- **Peripheral:** Use a docked bag of vancomycin 500mg/100ml

NB: If docked bag is unavailable, reconstitute each 500mg vial in 10ml water for injection and then dilute;

- **Central:** Draw up 1000mg vancomycin and make up to 100ml with sodium chloride 0.9% or dextrose 5%
- **Peripheral:** Draw up 500mg vancomycin and make up to 100ml with sodium chloride 0.9% or dextrose 5%

### Administration

**Loading Dose**

- Loading dose ≤ 1000mg: infuse over 1 hour.
- Loading dose > 1250mg & <2000mg: infuse over 2 hours.
- Loading dose ≥ 2000mg: infuse over 3 hours.
Maintenance Continuous Infusion

<table>
<thead>
<tr>
<th>Vancomycin dose per hour (mg/hr)</th>
<th>Central Line infusion rate (ml/hr)</th>
<th>Peripheral line infusion rate (ml/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>146</td>
<td>14.6</td>
<td>29.2</td>
</tr>
<tr>
<td>125</td>
<td>12.5</td>
<td>25</td>
</tr>
<tr>
<td>104</td>
<td>10.4</td>
<td>20.8</td>
</tr>
<tr>
<td>83</td>
<td>8.3</td>
<td>16.6</td>
</tr>
<tr>
<td>63</td>
<td>6.3</td>
<td>12.6</td>
</tr>
<tr>
<td>42</td>
<td>4.2</td>
<td>8.4</td>
</tr>
<tr>
<td>21</td>
<td>2.1</td>
<td>4.2</td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Please note: at low infusion rates eg 2.1ml/hr the vancomycin infusion must be replaced after 24 hours with a new infusion bag.

Compatibility

Whenever possible use a separate lumen for the vancomycin infusion. Y site compatibility information for vancomycin at a concentration of 10mg/ml is shown below:

**COMPATIBLE**
- Aciclovir sodium
- Atracurium
- Ciprofloxacin
- Dobutamine
- Esmolol
- Insulin, soluble
- Magnesium sulphate
- Midazolam
- Morphine Sulphate
- Noradrenaline
- Remifentanil

**INCOMPATIBLE**
- Albumin
- Aminophylline
- Drotrecogin Alfa
- Frusemide
- Heparin
- Hydrocortisone sodium succinate
- Tazocin

Please note that this list is non-exhaustive. Information on compatibilities and incompatibilities of vancomycin with other drugs are also available. If needed, contact the Pharmacist for advice.

Monitoring

Send a plasma level to Microbiology every morning. Label the sample “Continuous Vancomycin Level”. If vancomycin treatment is started within 6 hours of the usual 0800hrs level then wait until the next morning to take a level and act on. Adjust the daily dose depending on the level and check with the clinician and Pharmacist. Infusion rate changes should be made according to the table below:

<table>
<thead>
<tr>
<th>Vancomycin Serum Level (mg/L)</th>
<th>Rate Change Required</th>
<th>Infusion Rate Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>Increase the rate by 21mg/hr</td>
<td>Increase infusion rate to next level up in the table (see maintenance infusion table above)</td>
</tr>
<tr>
<td>15 – 25</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>&gt;25</td>
<td>Decrease the rate by 21mg/hr*</td>
<td>Reduce infusion rate to next level down on the table (see maintenance infusion table above)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>STOP infusion for at least 6 hours</td>
<td>Re-start at a reduced rate (as agreed with clinicians and Pharmacist)</td>
</tr>
</tbody>
</table>

*if current rate is 21mg/hr reduce to 10mg/hr.

Monitor for otoxicity and worsening renal function.
Cautions

Patients with renal impairment or history of deafness\(^6\). Avoid rapid infusion (see adverse effects). The risk of nephrotoxicity associated with continuous vancomycin infusion is markedly increased at a serum steady-state concentration \(>28\text{mg/L}\)\(^9\).

Adverse Effects\(^6\)

Nephrotoxicity, ototoxicity (discontinue if tinnitus occurs), blood disorders. Rapid infusion may cause severe hypotension (including shock and cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body (‘red man syndrome’) or pain and muscle spasm of the chest and back. Extravasation may cause tissue damage.

Instructions for discharge to ward

- Stop the infusion
- Divide the total daily vancomycin dose by 2, and re-prescribe as two 12-hourly iv doses
- Commence when the vancomycin level is predicted to be \(<10\text{mg/L}\)

References


Adapted from Guy’s and St. Thomas’ Intensive Care Units Guidelines for the use of vancomycin by continuous infusion. Giles L et al; October 2001.
Annex 6 Guidelines for Salvage of Infected Long Term or Skin Tunnelled Central Venous Catheters

Note: Line salvage is restricted to tunnelled catheters as non-tunnelled catheters are easily removed and replaced to reduce the risk of systemic infection

INTRODUCTION

The bacterial colonisation of central venous catheters presents a significant risk to the patient and a challenge to modern healthcare. Removal of colonised catheters is the most effective means of eradicating the infection, but this can mean removing the only means of venous access in some patients.

In recent years there has been a move towards the use of antibiotic line locks which involves instilling 1-2 mls of concentrated antibiotic into each lumen of the catheter and leaving it for a prescribed amount of time before removal, this process may be repeated for 1-2 weeks or longer if deemed necessary [Berrington and Gould 2001, Segarra-Newnham and Martin-Cooper 2005, Curtin et al 2003].

The protocol will describe measures to be taken when attempting catheter salvage, however it will not be suitable for all situations and assessment of the individual patients circumstances and medical condition will need to be undertaken prior to commencement.

Note: Central venous catheters will be referred to just as catheters throughout this document

USE OF ANTI-BACTERIAL 'LOCKS' IN TREATING INFECTIONS IN CENTRAL VENOUS ACCESS DEVICES

SALVAGE OF LINES

Note: There are many different types of catheters in use and the internal fill volume varies. The volume instilled should be no greater than the internal volume of the catheter. The antibiotic lock will usually be supplied by pharmacy and each syringe will contain antibiotic at the required mg per ml so each line will receive the optimum amount of antibiotic irrespective of the internal capacity. Only syringes of 10ml and above must be used.

TREATMENT REGIMEN

Fungal infections - These infections DO NOT RESPOND to conservative management – Removal of the catheter is required followed by at least 14 days of systemic antifungal treatment

Staphylococcus aureus - Conservative treatment is NOT ADVISED. Recommended action is immediate removal of the catheter and 14 days systemic anti-Staphylococcal treatment.

Gram positive organisms - Vancomycin lock 2mg per ml = total volume in syringe 2.5mls.

Gram negative organisms - Gentamicin lock 1mg per ml = total volume in syringe 2.5mls.
(If 1mg/ml not available, use 10mg/ml short term until a 1mg/ml solution can be sourced from Pharmacy.)

Gentamicin resistant infections - seek specialist advice

NB - All drugs to be used twice a day with a minimum dwell time of six hours and for a minimum of 7 days; preferred treatment duration is 14 days.
2nd Line treatment

A combined Vancomycin and Gentamicin lock can also be used

3rd Line treatment

**Tobramycin** - 1mg per ml BD [total volume in syringe 2.5ml]

**Amikacin** - 3mg per ml BD [total volume in syringe 2.5ml]

**Ciprofloxacin** - 2mg per ml BD [total volume in syringe 2.5ml]

NB: The information above is meant as a guide only. For further advice contact the Consultant Microbiologist.

REFERENCES

Berrington A Gould F K [2001] Use of antibiotic locks to treat colonized central venous catheters *Journal of Antimicrobial Chemotherapy* 48, pp597-603


Annex 7  **Antifungals**  
Antifungal agents are high cost drugs, and account for a disproportionate amount of the antimicrobial budget.

**BNF prices per day assuming 70kg patient**

<table>
<thead>
<tr>
<th>Antifungal Agent</th>
<th>Daily dose</th>
<th>BNF price PER DAY</th>
<th>BNF price 14 days course</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV fluconazole</td>
<td>400mg once daily</td>
<td>£55.64</td>
<td>£778.96</td>
</tr>
<tr>
<td>Oral fluconazole</td>
<td>400mg once daily (max routine dose)</td>
<td>£3.04</td>
<td>£42.56</td>
</tr>
<tr>
<td>IV voriconazole</td>
<td>4mg/kg twice daily maintenance dose (loading dose 6mg/kg first 24hrs)</td>
<td>£309.60</td>
<td>£4334.49</td>
</tr>
<tr>
<td>Oral voriconazole</td>
<td>200mg twice daily maintenance dose, (400mg twice daily loading dose)</td>
<td>£78.77</td>
<td>£1339.04</td>
</tr>
<tr>
<td>IV caspofungin*</td>
<td>70mg loading dose</td>
<td>£416.78</td>
<td>£4676.49</td>
</tr>
<tr>
<td>IV caspofungin*</td>
<td>50 mg once daily maintenance dose</td>
<td>£327.67</td>
<td></td>
</tr>
<tr>
<td>IV Ambisome</td>
<td>3mg.kg rounded 200mg</td>
<td>£386.76</td>
<td>£5414.64</td>
</tr>
<tr>
<td>IV Ambisome</td>
<td>5mg/kg once daily 350mg</td>
<td>£676.83</td>
<td>£9475.62</td>
</tr>
</tbody>
</table>

* Echinocandins are high cost drugs usually governed by supra-regional contracts. As such the compound in stock may vary from time to time. The appropriate dose of each compound is as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Loading Dose</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anidulafungin</td>
<td>200mg od</td>
<td>100mg od</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>70mg od</td>
<td>50mg od (up to 80kg body weight) 70mg od (&gt;80kg body weight)</td>
</tr>
</tbody>
</table>

**INVASIVE FUNGAL INFECTION**

**Sepsis syndrome associated with yeast/fungaemia**

*First Line:* Intravenous echinocandin* for 14 days

*Second Line:* Contact Consultant Microbiologist

If candida is sensitive to Fluconazole, change to Fluconazole iv 400mg od.

Change all indwelling lines. DO NOT RAILROAD. Perform fundoscopy to check for retinal deposits. Echocardiogram strongly advised. Repeat blood cultures at the end of therapy.

**Intravenous Line Infection**
These infections do not respond to antifungal treatment alone. The line must be removed.

**First Line:** Intravenous echinocandin* for 14 days

**Second Line:** Contact Consultant Microbiologist

If candida is sensitive to fluconazole, change to fluconazole 400mg iv od to complete 14-day course.

Discuss oral switch with Consultant Microbiologist.

### Candida meningitis

**First Line:** 

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambisome (liposomal amphotericin B)</td>
<td>3 – 5 mg/kg od</td>
</tr>
<tr>
<td>(<strong>PLUS</strong>)</td>
<td></td>
</tr>
<tr>
<td>Flucytosine</td>
<td>100mg/kg per day po in 4 divided doses (ie 25mg/kg per dose)</td>
</tr>
</tbody>
</table>

Contact Consultant Microbiologist for advice

### Cryptococcal meningitis (HIV or solid organ transplant recipient)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambisome (liposomal amphotericin B)</td>
<td>3 – 5 mg/kg od</td>
</tr>
<tr>
<td>(<strong>plus</strong>)</td>
<td></td>
</tr>
<tr>
<td>Flucytosine</td>
<td>100mg/kg per day po in 4 divided doses (ie 25mg/kg per dose) for at least 14 days,</td>
</tr>
<tr>
<td>(<strong>followed by</strong>)</td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>400mg po od for a minimum of 8 weeks.</td>
</tr>
</tbody>
</table>

### Cryptococcal meningitis (Patients without HIV or organ transplant recipient)

Contact Consultant Microbiologist for advice.

- **ASPERGILLOSIS**

### Pulmonary

Refer to Respiratory Physician.

#### Allergic bronchopulmonary aspergillosis (ABPA)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole</td>
<td>6mg/kg iv 12-hourly first 24 hours then 4mg/kg 12-hourly (oral switch 200mg 12-hourly)</td>
</tr>
</tbody>
</table>

**Second Line:** Itraconazole 200mg od

### Aspergilloma

**First Line:** Surgical removal
Before prescribing any antimicrobial, check for allergies, drug interactions & contraindications

### Second Line
- Itraconazole 200mg od
  (The role of medical therapy in aspergilloma is uncertain - discuss with Consultant Microbiologist.)

### Invasive pulmonary aspergillosis associated with neutropenia

<table>
<thead>
<tr>
<th>First Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole 6mg/kg iv 12-hourly first 24 hours</td>
</tr>
<tr>
<td>then 4mg/kg 12-hourly</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liposomal Amphotericin (Ambisome) 3 – 5mg/kg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Third Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous echinocandin*</td>
</tr>
</tbody>
</table>

### Sinusitis

Refer to ENT for consideration of debridement / washout.

<table>
<thead>
<tr>
<th>First Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole 6mg/kg iv 12-hourly first 24 hours</td>
</tr>
<tr>
<td>then 4mg/kg 12-hourly</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous echinocandin*</td>
</tr>
</tbody>
</table>

### Otomycosis

Clotrimazole 1% otic solution, refer ENT for aural toilet

### SUPERFICIAL CANDIDIASIS

#### Oral Candida (“Thrush”)

<table>
<thead>
<tr>
<th>Non-immune suppressed patient (including inhaled steroids, diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Line:</td>
</tr>
<tr>
<td>Miconazole oral gel until 2 days after symptoms resolve, up to 7 days</td>
</tr>
</tbody>
</table>

| Second Line:                                                        |
| Nystatin suspension until 2 days after symptoms resolve, up to 7 days |

| If extensive or severe:                                             |
| Fluconazole 50mg po 24-hourly for 7 days                           |

<table>
<thead>
<tr>
<th>Immune suppressed patient (e.g. long term oral steroids, HIV, DMARDs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Line:</td>
</tr>
<tr>
<td>Miconazole oral gel until 2 days after symptoms resolve, up to 7 days</td>
</tr>
</tbody>
</table>

| Second Line:                                                        |
| Nystatin suspension until 2 days after symptoms resolve, up to 7 days |

| If extensive or severe:                                             |
| Fluconazole 50mg to 100mg po 24-hourly for 7 days                  |

### Female Genital Candida
Uncomplicated

First Line: Clotrimazole 500mg vaginal pessary plus 2% topical cream (Canesten combi)

Second Line: Fluconazole 150mg po

Pregnancy

First Line: Clotrimazole 500mg vaginal pessary plus 2% topical cream (Canesten combi)

Do NOT use oral antifungals such as fluconazole.

Immune Suppressed

First Line: Fluconazole 150mg po 7 days

Severe

First Line: Fluconazole 150mg po 2 doses 3 days apart

Second Line: Clotrimazole 500mg vaginal pessary plus 2% topical cream (Canesten combi) repeated 3 days apart

Candida – Skin Infection (Intertrigo)

First Line: Clotrimazole 1% cream - apply 2-3 times daily. Add mild corticosteroid cream if itch is problematic

Second Line: Fluconazole 50mg po od 14 days if severe

Candida isolated from clinical specimens from patients without immune suppression

Urine: Seek genital thrush and treat as guidelines.

Sputum: Seek oro-pharyngeal thrush. Review steroid inhaler technique if applicable. Treat as per guidelines.

 Dermatophytosis/Skin Infections

Athlete’s Foot

First Line: Clotrimazole 1% cream maximum 7 days if combined with steroid (e.g. Canesten HC)

Second Line: Terbenafile 1% cream

If severe: Terbenafile 250mg po od 2-6 weeks.
**Fungal Nail Infection**

*First Line:* Amorolfine 5% nail lacquer  
6 months for fingernail infection, 9-12 months for toenail infection.

*Second Line:* Terbinafine 250mg od  
6 - 12 weeks for fingernail infection, 3-6 months for toenails.

**Fungal Skin Infection – Scalp (‘Ringworm’)**

Suspected kerion (pustular boggy mass) – refer to dermatology

*Patient lives in an urban area:* Terbenafine 250mg od.

*Patient lives in a rural area:* Griseofulvin 500mg od.

PLUS

*First Line:* Ketoconazole 2% shampoo. Apply od to affected area for 14 days. Lather, leave on for five minutes, rinse thoroughly.

*Second Line:* Selenium sulphide 2.5% shampoo (off label). As above, with 10 minute contact time, 14 days.

*Once culture results are known:*  
If *Trychophyton tonsurans* – **Terbinafine** 250mg od 4 weeks  
If *Microsporum* spp – **Griseofulvin** 500mg od 8 – 10 weeks

**Fungal Skin Infection – Body & Groin**

*First Line:* Clotrimazole 1% cream

*Second Line:* Consider oral antifungal treatment if extensive:

Terbinafine 250mg od 4 weeks OR  
Griseofulvin 500mg od 8 – 10 weeks OR  
Itraconazole 100mg od for 15 days or 200 mg bd for 7 days

**Pityriasis versicolor**

*First Line:* Ketoconazole 2% shampoo. Apply od to affected area for 5 days. Lather, leave on for five minutes, rinse thoroughly

*Second Line:* Selenium sulphide 2.5% shampoo (off label). As above, with 10 minute contact time, 7 days.

*If only small area involved:* Clotrimazole 1% cream 2 -3 weeks.

**Note:** Pigmentation persists for several weeks after yeasts have been eradicated
References

BASHH UK guideline on the management of vulvovaginal candidiasis (2007)  

British National Formulary September 2013


Lincolnshire joint formulary http://www.lincolnshirejointformulary.nhs.uk/  Accessed September 2013

Mandell, Douglas and Bennett’s Principles and practice of infection diseases. 6th edition 2005


Annex 8   Increased Dosage Regimens Including Out of Use/Off-Label Dosage (BNF) for Restricted Antibiotics

Introduction

There is a potential situation where there is a need to administer an antibiotic where we have to increase the dose to a level that is classed as "off-label dose". Although this might be a rare situation, unclear guidance and unnecessary delays in antibiotic dispensing and treatment could compromise a critically ill patient and possibly lead them to an adverse outcome. The "off-label dose" antimicrobials listed in this annex are not available without prior consultation with the Consultant Microbiologist. This consultation and the advice received, should be documented in the patients notes and the prescription sheet annotated "on Microbiologist Advice", with the name of the Microbiologist consulted included.

1. Daptomycin

EMA (European Medicines Agency) and FDA indication for daptomycin are complicated skin and soft-tissue infections and *S. aureus* bacteraemia, including those with right-sided endocarditis, caused by MSSA and MRSA. Non approved uses include treatment in osteomyelitis, diabetic foot infection, septic arthritis, surgical wound infections and hepatic abscess. For daptomycin the BNF states a maximum dose of 6 mg/kg daily dose; however a dose up to 12mg/kg might be required. Daptomycin has been studied in healthy volunteers at doses exceeding the current FDA-approved dosages including 12 mg/kg once daily and no electrocardiographic abnormalities or electrophysiological evidence of muscle or nerve toxicity was noted, and none of the patients experienced myalgia. Furthermore high-dose daptomycin therapy shows a satisfactory toxicity profile even in severely ill patients with multiple comorbidities, and may favorably compete with vancomycin, especially concerning the risk of induced nephrotoxicity.

- Cautions: interference with assay for prothrombin time and INR—take blood sample immediately before daptomycin dose. Caution in severe hepatic impairment.
- Interactions: Check BNF.
- Side effects: Check BNF.

Daptomycin monitoring and review

- Monitor renal function if eGFR less than 80 mL/minute/1.73 m²; use normal dose every 48 hours if eGFR less than 30 mL/minute/1.73 m².
- Monitor creatine kinase and liver function tests before treatment and then weekly during treatment (more frequently if creatine kinase elevated more than 5 times upper limit of normal before treatment, or if receiving another drug known to cause myopathy (preferably avoid concomitant use), or if eGFR less than 80 mL/minute/1.73 m2). If unexplained muscle pain, tenderness, weakness, or cramps develop during treatment, measure creatine kinase every 2 days.
- Monitor for myalgia, muscle weakness. Myositis may occur uncommonly and rhabdomyolysis is very rare. Discontinue daptomycin if unexplained muscular symptoms and creatine kinase elevated markedly (more than 5-7 times upper limit).

References:


2. Colistimethate Sodium

Intravenous administration of Colistimethate Sodium (CMS) should be reserved for Gram-negative infections resistant to other antibiotics. CMS major adverse effects are dose-related neurotoxicity and nephrotoxicity. Doses should always be expressed in IU of colistimethate sodium (1mg colistin base activity is contained in 2.4mg colistimethate sodium which is equivalent to 30,000 IU of colistimethate sodium).

For colistin sulfoxymethate sodium (colistimethate sodium) the BNF states a maximum 2 million unit’s dose 3 times daily, however in critically ill patient a loading dose of 9 million units is more likely required with a maintenance dose of 4.5 million units every 12 hours. Several expert frameworks have already addressed the optimisation of the clinical use of colistin leading to consensus advice and guidelines. Many expert frameworks are in agreement that the traditional dosing regimens for colistimethate sodium does not attain serum concentrations that would be sufficient for the treatment of infections caused by pathogens with MIC>0.5mg/L and therefore a high loading dose and high doses regimens are required. According to the European Medicines Agency complete review of polymyxin-based medicines recommendations issued for safe use in patients with serious infections resistant to standard antibiotics (document EMA/643444/2014, 24 October 2014) "Based on the limited available evidence the recommended dose in adults is 9 million IU daily in 2 or 3 divided doses as a slow intravenous infusion; in critically ill patients a loading dose of 9 million IU should be given. Doses should be reduced according to creatinine clearance in patients with renal impairment".

- Contraindications: Myasthenia Gravis
- Cautions: Acute porphyria
- Interactions: Avoid other drugs which may potentiate nephrotoxic including antibiotics (e.g. gentamicin, vancomycin, amphotericin, rifampicin), neuromuscular blocking agents. Check BNF.
- Side-effects: Neurotoxicity especially with high doses e.g. apnoea, peri-oral and peripheral paraesthesia, vertigo, headache, muscle weakness; rarely vasomotor instability, slurred speech, confusion, psychosis, visual disturbances, nephrotoxicity, rash. For more, check BNF.

**Table 1: Loading Dose (Adults):**

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Loading Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 50kg</td>
<td>9 million units (MU)</td>
<td>In obese patients (BMI&gt;30) dosing should be based on Ideal Body Weight. Use of actual body weight in these patients is associated with increased incidence of nephrotoxicity. The loading dose is unaffected by renal impairment.</td>
</tr>
<tr>
<td>50kg or less</td>
<td>6 million units (MU)</td>
<td></td>
</tr>
</tbody>
</table>

*Source: High Dose Colistimethate Sodium (Colistin) in Adults, Consensus Guidance, Scottish Medicine Consortium and Scottish Antimicrobial Prescribing Group, NHS Scotland, 2014.*

**Table 2: Maintenance Dose (Adults):**

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Dose and Frequency</th>
<th>Starting time after loading dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>4-5 MU every 12 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td>20-50</td>
<td>4-5 MU every 24 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td>&lt;20</td>
<td>4-5 MU every 48 hours</td>
<td>48 hours</td>
</tr>
<tr>
<td>Patient undergoing CVVHDF</td>
<td>4-5 MU every 24 hours</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

*Source: High Dose Colistimethate Sodium (Colistin) in Adults, Consensus Guidance, Scottish Medicine Consortium and Scottish Antimicrobial Prescribing Group, NHS Scotland, 2014.*
**Colistimethate Sodium monitoring and review**

- Renal function should be monitored daily for the first week and adjustments made if required. If the patient’s renal function is stable monitoring can be reduced to every 2-3 days.

- Therapeutic drug monitoring (monitoring plasma concentrations) of colistin may be a useful strategy for the prediction and prevention of AKI in patients undergoing colistimethate sodium therapy. Plasma levels can be measured at Bristol Southmead laboratory. Therapeutic drug monitoring is recommended every 2 days or every 5-7 days assuming initial results are within the expected range and the patient’s renal function is stable. N.B. Other antibiotics can interfere with the assay therefore the laboratory need to know the full list of antibiotics the patient is receiving.

- The literature suggested trough (pre) levels of 2-6mg/L and peaks (post) of 5-15mg/L are based on 8 hourly intervals dosing, therefore carefully interpretation is required. The antimicrobial reference laboratory suggests a trough (pre) of 2-4 mg/L.

- Monitor for signs of neurotoxicity, e.g. apnoea, peri-oral and peripheral paraesthesia, vertigo, headache, muscle weakness; rarely vasomotor instability, slurred speech, confusion, psychosis, visual disturbances.

**References**


Annex 9  Sepsis Poster

MANAGEMENT OF INFECTIONS IN ADULT PATIENTS

BEFORE PRESCRIBING ANY ANTIMICROBIAL, CHECK FOR ALLERGIES, DRUG INTERACTIONS & CONTRAINDICATIONS

Anticipate each patient thoroughly taking into account:

- Ideal Body Weight (IBW)
- Renal Function
- Hepatic Function
- Past Medical History
- Drug hypersensitivities
- Recent antibiotic use

Ensure adequate bacteriological samples are taken prior to starting antimicrobial therapy.

**NEUTROPHILIC SEPSIS**

- *Pseudomonas aeruginosa* \( \beta \)-lactams iv *or* aminoglycosides iv

- *Staphylococcus aureus* \( \beta \)-lactams iv *or* vancomycin iv

- *Acinetobacter* \( \beta \)-lactams iv, amikacin iv

**SEPSIS OF UNKNOWN ORIGIN** (if origin is known please refer to the appropriate site-specific box below):

- *Escherichia coli* \( \beta \)-lactams iv *or* gentamicin iv

**SEPSIS SYNDROME**

- *If* penicillin allergic, *use* meropenem 1g (or 2g if severe) 8 hourly iv *or* gentamicin 7mg/kg IBW iv at frequency according to Hartford nomogram. (see Antibiotic Formulary)

- *If* penicillin allergic (severe), *use* vancomycin iv (see Antibiotic Formulary) + ciprofloxacin 500mg 8 hourly iv + metronidazole 500mg 8 hourly iv + gentamicin 7mg/kg IBW iv at frequency according to Hartford nomogram. (see Antibiotic Formulary)

**GASTROINTESTINAL INFECTIONS**

- Biliary tract: *Piperacillin/tazobactam* 4.5g 8 hourly iv

- Escherichia coli: *Ciprofloxacin* 1.25g 8 hourly iv

**UROSEPSIS**

- *Escherichia coli*: *Ciprofloxacin* 1.25g 8 hourly iv

**SOFT TISSUE INFECTIONS**

- *Staphylococcus aureus*: *Flucloxacillin* 2g 8 hourly iv

**BONES & JOINT INFECTIONS**

- *Staphylococcus aureus*: *Flucloxacillin* 2g 8 hourly iv

**COMMUNITY-ACQUIRED PNEUMONIA**

- CURB 0-1: Amoxicillin 500mg q 8 hourly po

- CURB 2: Amoxicillin 500mg q 8 hourly po + clarithromycin 500mg 12 hourly po

- CURB 3: Co-amoxiclav 1.2g q 8 hourly iv + clarithromycin 500mg 12 hourly iv po or or

- CURB 4: Severe allergy: Contact Consultant Microbiologist

**HOSPITAL-ACQUIRED PNEUMONIA**

- 5d onset: *Cefuroxime* 1.5g 8 hourly iv

**SUSPECTED ENDOCARDITIS** (initial antibiotic treatment)

- Take 3 sets of blood cultures over an hour end contact Consultant Microbiologist

- Native valve: *Inderol - amoxicillin* 2g 4 hourly iv

- Prosthetic valve: *Vancomycin* (see Antibiotic Formulary) + gentamicin 7mg/kg IBW 12 hourly iv (NOT once daily regimen) + rifampicin 600mg 12 hourly iv or po

**Sepsis Alert**

- *Flucloxacillin* 2g 8 hourly iv

- *Ciprofloxacin* 500mg 8 hourly po (or 400mg 8 hourly iv) + metronidazole 600mg 12 hourly po or iv

- *Cefuroxime* 1.5g 8 hourly iv

- *Flucloxacillin* 2g 8 hourly iv + metronidazole 500mg 8 hourly iv (+ gentamicin 160mg sl iv if viable sputum)

**INFECTION site**

- *Flucloxacillin* 2g 8 hourly iv

- *Flucloxacillin* 2g 8 hourly iv + metronidazole 500mg 8 hourly iv (+ gentamicin 160mg sl iv if viable sputum)