Livewell Southwest

Antimicrobial Treatment Guidelines

Version No 4.4

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Notice to staff using a paper copy of this guidance

The policies and procedures page of LSW intranet holds the most recent version of this document and staff must ensure that they are using the most recent guidance.

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V.2,2	Reviewed	Nov 2010	Director of Infection Prevention & Control.	Reviewed no changes made
V.4.1	Reviewed by PHNT	April 2012	Dr Greig	See p.5.
V.4.2	Extended	October 2014	Infection Prevention & Control Nurse.	Extended no changes
V4.3	Extended and Updated	June 2016	A Hawke	Extended, Updated & formatted to LSW.
V.4.4	Extended	December 2016	Clinical Director of Pharmacy	Extended no changes

Livewell Southwest have adopted this policy and procedure from Plymouth Hospitals NHS Trust (PHNT).

Please note where reference is made to PHNT or PHNT staff this would also apply to Livewell Southwest (LSW)

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Antimicrobial Treatment Guidelines
Livewell Southwest
Version 4.1

April 2012
1.06.2013

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Amendments April 2012

- Changed first line treatment of chlamydial urethritis to single dose of azithromycin 1g with seven days of doxycycline as alternative. Doxycycline remains the preferred agent in combination treatment for PID

- Add the adapted Department of Health Stay *Smart then Focus* advice regarding antimicrobial selection and the need for a documented Antimicrobial Prescribing Decision

Part 1 How to use Antibiotics

Part 2 Specific guidance on the management of certain infections

***** No detail guidance is included here, refer to guidance noted under these headings

Antibiotics should be:

Administered only for as long as necessary

Reviewed daily and have a review date noted on the drug chart

Changed from IV to oral as soon as possible

Modified in the light of microbiological investigations

Adjusted according to renal and hepatic function

Part 1 General points regarding the safe and effective use of Antimicrobials

1. Introduction

This document is designed for use by staff of Livewell Southwest and lays out the guidelines for the treatment of common community and hospital acquired infections. Separate though complimentary primary care guidelines are available in the Plymouth Area Joint Formulary.

These guidelines are designed to be read in conjunction with other relevant treatment guidelines e.g. LSW Infection Control Policies, Plymouth Area Joint Formulary.
There is an abbreviated form of these guidelines available on Healthnet and miniaturised credit card guidelines available on request from Microbiology Department

2. The Perfect Prescription[1]

Do not start antibiotics in the absence of clinical evidence of bacterial infection

Prior to the Administration of antimicrobial therapy
Use guidelines

Use local guidelines to initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with life threatening infections. Where such policy does not exist employ antimicrobials in line with good evidence based practice

Restricted access antimicrobials

Antimicrobials with a restricted access must only be used in accordance with this policy or after discussion with a Microbiologist/attending Consultant. Where used under guidance this must be clearly documented in the notes

Document in the notes what you are doing and why

Document in medical notes: clinical indication, duration or review date, route and dose. Antibiotics are often continued unnecessarily because those caring for the patient do not have information indicating why the antibiotics were started and how long they were planned to be continued. This problem is compounded where primary responsibility for patient care is frequently transferred from one clinician to another. Ensure all antibiotic prescriptions are always accompanied by an indication and a clear duration. Where a review date cannot be safely applied ie unclear extent or type of infection a review date must be applied to the drug chart as soon as possible

Take samples before starting the antibiotics

Knowing the susceptibility of an infecting organism can lead to narrowing of broad-spectrum therapy, changing therapy to effectively treat resistant pathogens and stopping antibiotics when cultures suggest an infection is unlikely.

Ongoing Antimicrobial Use

Review the clinical diagnosis and the continuing need for antibiotics by 72 hours and make a clear plan of action - Antibiotics are generally started before a patient's full clinical picture is known and by 72 hours a re evaluation should take place and a de escalation of therapy considered (see section 3)

At 72 hours make and document an Antimicrobial Prescribing Decision.

The antibiotic prescribing decision options are Stop, Switch, Change and Continue

1. Stop antibiotics if there is no evidence of infection
2. Switch antibiotics from intravenous to oral
3. Change antibiotics – ideally to a narrower spectrum (de escalation), or broader if required
4. Continue, review and document again every 72 hours

The reasons for continuation of an IV antibiotic beyond 72 hours must be clearly documented in the notes, kept under regular review and reaffirmed every few days. Where ever possible the oral route is preferred to IV as this reduces complications and cost

Antimicrobial choices should be reviewed and amended if appropriate on receipt of results of microbiology tests which along with any prescription changes should be recorded in the patient notes

3. De escalation

As the cause of many infections on presentation is unclear and failure to effectively treat the causative organisms on presentation can lead to poorer clinical outcomes broad spectrum antimicrobial use is often appropriate. Once the cause of an infection is identified one can usually narrow the spectrum of the antibiotics and often change IV antibiotics to orals. This de escalation often leads to improved clinical outcomes and more rapid patient discharge

- Use broad spectrum antibiotics in line with these guidelines
- Ensure a suitable range of clinical specimens are taken before starting antimicrobials

- Where possible de escalate to narrow spectrum antibiotics as soon as safely possible

- Failure to take suitable specimens may mean that a patient remains on a broad IV agent for days to weeks. Oral options may not be possible if there is no supporting laboratory evidence to facilitate a safe switch

4. Intravenous/Oral Switch

A prompt switch from intravenous to oral therapy is desirable.
The benefits of a switch are**:**

- Patient preference and enables prompt discharge
- Avoids the morbidity associated with intravenous cannulation
- Reduces nursing time involved in drug preparation and administration
- Avoids toxicities associated with IV solution components
- Cost

Only general guidance can be offered regarding when a switch is appropriate and clinical judgement needs to be applied.

Conditions for which an oral switch is generally not appropriate**:**

- Endocarditis
- Meningitis and encephalitis
- Mediastinitis
- Neutropenic fever (except in carefully selected cases under the care of a Consultant with experience in the management of such patients)

Criteria to select eligible patients [modified from ref 2]

These criteria in general should all be satisfied though each patient should be assessed on a case by case basis

- Patient is not septicaemic and the condition is not considered life threatening

- At least 48 hours of IV therapy

- Signs and symptoms of infection indicate clinical improvement

- Temperature is less than 38°C

- If initially elevated, white blood cell counts are normal or falling

- Gastrointestinal absorption is likely to be normal eg absence of vomiting, no continuous NG suction, no GI motility abnormalities, no short bowel syndrome

etc

- Availability of an adequate oral antibiotic (see below)

Antibiotics considered suitable for early IV/Oral switch

Antibiotic	% Absorption of oral formulation[3]
Levofloxacin	>95
Metronidazole	>95
Clindamycin	70-85
Linezolid	>95
Co-amoxiclav	60
Flucloxacillin	>60
Amoxycillin	50-70
Doxycycline	80-95

5. Duration of Treatment

Most infections resolve with short courses of antibiotics. See part 2 for guidance on treatment duration for simple infections

- In most cases the anticipated duration of antibiotic should be noted when the prescription is written

- Changes to the duration of treatment must be noted on the drug chart when moving to oral treatment from IV i.e. after 2 days IV of a 7 day course, the new oral prescription should have a 5 day review

- Where there is no noted duration Ward Pharmacists are encouraged to place one week reviews on the drug chart. It is the attending team's responsibility to regularly review drug charts and to re-prescribe if a longer antibiotic course is required

6. Active Management of Antibiotic use

The policy at LSW is to control antibiotic use via a closed, restrictive formulary supported by evidence based polices, education, prospective day to day review of antibiotic use and regular audit. Elements of this include:

- Closed/restrictive formulary with broad-spectrum antibiotics use including third generation cephalosporins and quinolones discouraged
- Regular review of antibiotic prescriptions by Pharmacy staff to ensure appropriate antibiotics are being used and to facilitate prompt IV/PO switching with referral to a microbiologist where needs be
- On-going audit and review of drug charts with regular feedback to prescribers of antibiotic use and notification of errors in antibiotic use
- New prescriptions of broad spectrum antibiotics are reviewed on a regular basis by a Consultant and a pharmacist
- Medical and Nursing staff are targeted on a regular or opportunistic basis for teaching on the general principles of antibiotic prescribing

7. Restricted antibiotics and off –formulary prescribing

Broad-spectrum antibiotics such as carbapenems, daptomycin, tigicycline and linezolid are vital agents in the treatment of severe infection. Overuse will lead to a loss of efficacy. Restrictions are placed on the use of certain agents.

- Restricted antibiotics are noted in the Formulary with a triangle Δ
  These should not be used except where Trust policy states otherwise without first seeking the advice of a Microbiologist or at the direction of the attending Consultant. In such cases the name of the consultant must be documented in the notes
- Ward Pharmacists will challenge inappropriate use of restricted agents
- The use of certain broad spectrum antibiotics are reviewed on a regular basis by a consultant and further assistance is available from the on call Microbiologist

Restricted agents (Marked in the formulary with Δ)

Beta lactams		
Ceftriaxone	Ceftazidime	Aztreonam
Meropenem	Ertapenem	
Other antibiotics		
Amikacin	Colistin	Linezolid
Ciprofloxacin	Daptomycin	Tigecycline
Antifungals		
Itraconazole	Voriconazole	Posaconazole
Caspofungin	Amphotericin	

Antibiotics not on the Formulary

New Admissions

Where a patient is admitted from a referring hospital on a non-formulary antibiotic an alternative formulary antibiotic can usually be identified. It is **NOT** appropriate to simply leave a patient on a non-formulary antibiotic. Further advice is available from the Ward Pharmacist or the on call Microbiologist

Applications for new antibiotics

There are few instances where antibiotics other than those on the formulary are required. Where this is the case discuss with on call Microbiologist

8. Beta lactam allergy

Penicillin allergy

Type 1 anaphylactic reaction, urticarial rash or Stephens-Johnson syndrome
Patients with a history of type 1 hypersensitivity reaction (urticaria, angioedema, anaphylaxis) or Stephens-Johnson syndrome precipitated by beta lactam antibiotics (penicillins, cephalosporins, carbapenems eg meropenem/ertapenem or aztreonam) should avoid all beta lactams. In cases where such agents are essential and no alternative exists contact a consultant Microbiologist or Immunologist to discuss

Non-urticarial rash to penicillins

Patients with non-urticarial rash allergies to penicillins may receive a cephalosporin in a controlled environment. The risk of subsequent rash allergy to a cephalosporin is likely to be less than 5%. The risk of anaphylaxis to cephalosporins remains small but one should be prepared for such reactions. The risk of allergy to carbapenems and aztreonam in individuals with a rash allergy to penicillins is small

Allergy to other beta lactams

Where there is a documented allergy to non-penicillin beta lactams the risk of cross-reactions with related antibiotics (see BNF for groupings of antibiotics) needs to be discussed with the on call Microbiologist

9. Antibiotics in Pregnancy

The safety of many antimicrobials in pregnancy has not been established. See BNF regarding safety. Where uncertainty exists contact the on call Microbiologist. The table below is designed to be a reminder of common antibiotics but when prescribing in

pregnancy it is the duty of the prescriber to satisfy themselves regarding the safety of individual agents.
Further assistance is available from PHNT drug information and the regional drug and Therapeutics centre at http://www.nyrdtc.nhs.uk/Services/teratology/teratology.html

Safe	Avoid
Penicillins (see below regarding co-amoxiclav)	Tetracyclines including tigecycline
Cephalosporins	Trimethoprim (D/W on call Microbiologist if no alternatives available)
Erythromycin	Quinolones including levofloxacin
Nitrofurantoin (avoid in the first trimester and after 36 weeks gestation)	Metronidazole (probably safe during 2nd & 3rd trimester if high dose formulation avoided)
	Aminoglycosides (except in life threatening infections)
	Co-amoxiclav has been associated with neonatal NEC on occasions. Avoid throughout pregnancy. Discuss with Microbiologist if no other options exist

10. Use of Teicoplanin, Vancomycin and Gentamicin

[i] Gentamicin administration

Single daily dosing is recommended in most circumstances. Only trough serum levels need to be monitored. Appropriate dosing and correct monitoring reduce risk of nephrotoxicity. In individuals with significant renal impairment eg GFR <20 consider non aminoglycoside alternatives

a. Initial dose

5mg/kg. If the patient weighs over 100kg a dosing correction needs to be made. In such cases see local guidance *Use of antibiotics in Obesity*. In renal failure alternative agents are usually available, discuss with the on call Microbiologist

b. Second dose

A trough gentamicin level must be measured before giving the second dose.

The trough level should be taken 22-24 hours after the first dose. Mark clearly on the request form when the sample was taken and when the last dose was given. Await result before determining the next dose of gentamicin as follows:

Gentamicin level	**Action to be taken**
< 1 mg/l	Give dose and re-assay before every 3rd dose if normal creatinine and stable renal function, otherwise re-assay before every dose
> 1 mg/l	Extend the dosing period GFR 20-40 dose every 48 hours. Take trough level prior to the next dose and redose if <1 GFR <20 Take trough level at 48 hours and then every 24 hours until less than 1 then redose Where GFR is reduced all aminoglycosides are best avoided (excepting patients without salvageable renal function eg on long term HD)

c. Continuation

Review need for long-term treatment no more than 72 hours after first dose. If infection is unconfirmed stop antibiotic treatment. If treatment continues, monitor serum creatinine twice weekly and gentamicin levels as above

d. Twice daily gentamicin dosing in endocarditis

Gentamicin is indicated for some streptococcal and enterococcal infections at a dose of 1-1.5mg/kg (up to a maximum of 120mg bd) every 12 hours. If renal function is impaired eg GFR<40 discuss with the on call microbiologist. Take levels immediately before (trough) and one hour after the dose and send both samples to the laboratory together.

Pre dose levels: <1mg/l
Post dose levels: 3-5mg/l

[ii] Vancomycin administration[6]

Target pre-dose level should be 10-20 mg/l

Initial doses should be based on total patient weight with subsequent doses based on renal function.

The eGFR released with Chemistry reports assumes the patient to be 70kg so if the patient's weight is significantly different from 70kg the renal function must be recalculated using total body mass as the model upon which dosing is based has used the CG equation to incorporate dose and dosing interval.
Use:http://www.nuh.nhs.uk/nch/antibiotics/Renal%20impairment/clcrcalc.asp

a. Load all patients as noted below

b. Further doses depend on current renal function. For large patient ie mass >100kg discuss maintenance dose with the on call Microbiologist

Loading dose
Calculate according to total body weight

Weight (kg)	Dose (mg)
>90	2000
60-90	1500
<60	1000

Maintenance doses (start 12 hours after loading dose)

GFR	Dose
>90	1500mg every 12 hours
75-90	1000mg every 12 hours
40-75	750mg every 12 hours

Monitor level 1-2 hours before fourth dose, and twice weekly thereafter or more frequently if serum concentrations are out of the normal range. If renal impairment (GFR <40) or level >20mg/l discuss with microbiologist.

[iii]. Teicoplanin administration

Load with three doses 12 hours apart (even in renal impairment). Teicoplanin comes in 400mg and 200mg vials, when calculating doses round up to the nearest 200mg

Standard regimen: (excepting endocarditis and bone and joint infections)

Load with three 12 hourly doses then convert to once daily maintenance teicoplanin starting with the fourth dose on day 3

Loading dose
6mg/kg for three 12 hourly doses

Maintenance dose

GFR greater >60ml/hr	6mg/kg
GFR 40-60ml/hr	6mg/kg on day 3 and then 3mg/kg from day 4
GFR <40ml/hr	6mg/kg on day 3 and then 2mg/kg from day 4

Rule of thumb dosing for patients weighing 50-100kg

If GFR is greater than 60ml/hr then those weighing 50-75kg should receive 400mg and those weighing 75-100kg should receive 600 mg for loading and maintenance doses. Patients with GFR<60 or who weigh <50Kg >100Kg must have their dose calculated according to weight

High dose regimen eg Endocarditis and bone and joint infections

Loading dose

12mg/kg for three 12 hourly doses

Maintenance dose

GFR greater >60ml/hr	6mg/kg twice daily
GFR 40-60ml/hr	6mg/kg twice daily on day 3 then 3mg/kg twice daily from day 4
GFR <40ml/hr	Discuss regimen with a microbiologist

11. Avoidance of antibiotics associated with C. difficile

Any antibiotic can in the susceptible lead to C. difficile disease though some are more closely associated than others.

High Risk	**QUINOLONES CLINDAMYCIN CEPHALOSPORINS**
Moderate risk	co-amoxiclav amoxicillin piperacillin/tazobactam meropenem/ertapenem vancomycin
Low risk	tetracyclines gentamicin trimethoprim flucloxacillin metronidazole nitrofurantoin

There are few indications for cephalosporins and quinolones beyond CNS infections and treatment of the penicillin allergic

Part 2 Specific Guidance of the management of certain infections

1. Sepsis of Unknown Origin

The antibiotic management of sepsis of unknown cause relies on preventing an irreversible deterioration in the patient's condition pending results of specific investigations. The majority of septic patients have signs and symptoms that suggest the primary infectious cause. Common diagnostic uncertainties are between pneumonia and UTI. Treatment of severe pneumonia will treat most community acquired UTIs. An important aspect of management of SUO is the inclusion of an anti-MRSA agent where MRSA is likely.

Up to one quarter of community associated gram negative bacteraemias are due to co-amoxiclav resistant strains so consider initial once daily gentamicin, which can be stopped if the isolated bacterium is co-amoxiclav sensitive.

A prompt patient improvement often follows successful resuscitation and initiation of gentamicin. If there is a clinical improvement but the bacteriological cause for the sepsis remains unclear continue once daily gentamicin until one is confident that the clinical improvement is not due solely to the gentamicin

[a]. Community associated

[i]. Antibiotics Preferred

Co-amoxiclav 1.2g tds IV
Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use piperacillin/tazobactam or in the event of past history of ESBL or admission from residential care, meropenem in the first instance

Alternative

Levofloxacin 500mg bd and metronidazole tds (both preferably oral)
Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use meropenem 1g tds IV providing no severe allergy to beta lactams (see part 1 section 6) otherwise contact the on call Microbiologist

Consider teicoplanin in those at risk of MRSA infection especially in the presence of severe sepsis

[b]. Hospital or healthcare associated (includes residential/inpatient care, those

with indwelling IV lines and frequent contact with in patient services)

[i]. Antibiotics Preferred

Piperacillin/tazobactam 4.5 g tds IV plus teicoplanin IV (unless MRSA excluded as a cause)
Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use meropenem 1g tds IV plus teicoplanin IV

Alternative

Levofloxacin 500mg bd, metronidazole tds (both preferably oral) and teicoplanin IV (unless MRSA excluded as a cause). Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use meropenem 1g tds IV in place of levofloxacin providing no severe allergy to beta lactams (see part 1 section 6) otherwise contact the on call Microbiologist

In patients admitted with severe sepsis from residential care or previously infected with an ESBL bacterium consider replacing co-amoxiclav, piperacillin/tazobactam or levofloxacin and metronidazole with meropenem and discuss with on call Microbiologist

[ii]. Microbiological Sampling

Blood cultures
Baseline CRP
Urinalysis and culture if positive
Screen for MRSA carriage, if using an anti-MRSA agent stop this if screens are negative

[iii] Oral switch

Not applicable, depends on ultimate underlying cause

[iv]. Duration

Not applicable, depends on ultimate underlying cause

[c]. Specific causes

Neutropenia	See guideline on Trustnet

Past history of MRSA	Include teicoplanin empirically
Residence in Nursing Home/ Recent hospitalisation Past history of ESBL infection (see PIMS)	Treat as for healthcare associated infection (section 1b above) Meropenem 1g tds IV and contact a microbiologist

2. IV cannula associated sepsis

Peripheral cannula should be removed if suspected of being infected and no less frequently than every 72 hours

[i]. Antibiotics Preferred

Flucloxacillin 2g qds IV plus gentamicin (review gentamicin at 24 hours and stop if clear infection is due to a flucloxacillin sensitive bacterium).
If known/suspected to be infected with MRSA, treat mild non-bacteraemic infections with oral doxycycline and oral rifampicin or if septicaemic or previous MRSA isolates resistant to tetracyclines use teicoplanin and gentamicin

Review need for teicoplanin at 48-72 hours and consider substituting for flucloxacillin if no evidence of MRSA infection

Alternative

Replace flucloxacillin with teicoplanin

[ii]. Microbiology investigations

Exit site pus/wound swab
Culture the blood from a distant vein if septicaemic
Baseline CRP

[iii] Oral switch

Discuss on a case by case basis with a Microbiologist. If endocarditis considered unlikely/excluded and infection due to a sensitive staphylococcus an early switch to flucloxacillin 1g qds may be possible. If due to MRSA similar oral switches include clarithromycin 500mg bd or doxycycline 100mg od and rifampicin 300mg bd depending on sensitivities.
If due to other pathogens or endocarditis thought likely discuss with on call Microbiologist

[iv] Duration

Non bacteraemic infections	7 days or less
Bacteraemic	14 or more days if S. aureus isolated If offending line is promptly removed and no suspicion of underlying endocarditis or valvulopathy a foreshortened course of 5 or fewer days is possible in coagulase negative staphylococcal (CNS) infections[7] Infection due to other pathogens, discuss with on call Microbiologist

3. Urinary tract infection

If clinically stable consider awaiting Microbiological results pending treatment
Local rates of trimethoprim and co-amoxiclav resistance in uropathogens may exceed 30%. These regimens may not be suitable for severe bacteraemic disease which should be treated as for sepsis of unknown origin

All urinary catheters will eventually become colonised with bacteria, presence of bacteriuria is not synonymous with infection

An uncomplicated UTI is considered one affecting a female in the absence of

- Systemic sepsis
- Urinary catheter
- Upper urinary tract infection
- Structurally abnormal urinary tract

[a]. Uncomplicated UTI

[i]. Antibiotics Preferred

Trimethoprim 200mg bd PO or co-amoxiclav 1.2g tds IV (if unable to take orals)

Alternative

Oral nitrofurantoin modified release 100mg bd
MRSA UTI can usually be treated with oral trimethoprim, doxycycline or nitrofurantoin. If past history of ESBL infection use fosfomycin 3g PO single dose or nitrofurantoin 100mg bd depending on previous susceptibilities. An alternative regimen is ertapenem 1g od IV which if selected should be discussed with the on call Microbiologist

[b]. Complicated UTI

In the event of a UTI associated with an indwelling catheter consider if the catheter can be replaced especially if in place for longer than one week

[i]. Antibiotics Preferred

Trimethoprim 200mg bd PO or co-amoxiclav 1.2g tds IV (if unable to take orals)
If past history of ESBL infection use ertapenem 1g od IV and discuss with the on call Microbiologist

Alternative

Levofloxacin 500mg od (preferably oral)

MRSA UTI can usually be treated with oral trimethoprim or doxycycline.

[ii]. Microbiological Investigations

Mid stream or catheter urine whilst not on antibiotics
Blood culture if septic
Baseline CRP if septic

[iii]. Oral switch

Depending on the sensitivity of the isolated strain trimethoprim 200mg bd, doxycycline 100mg od, amoxicillin 500mg tds or co-amoxiclav 625mg tds are all options

[iv]. Duration

Uncomplicated

Trimethoprim	3 days
Nitrofurantoin	5 days
Fosfomycin	Single 3g dose

Complicated 7 days regardless of drug selected

4. Lower respiratory tract infections

See section [c] below when considering whether to add empirical anti MRSA treatment

[a]. Community acquired pneumonia[8]

Non-severe pneumonia

[i]. Antibiotics Preferred

Amoxycillin 1g IV or 500mg PO tds plus doxycycline 200mg loading PO followed by 100mg PO od

Alternative

Levofloxacin 500mg od (preferably oral)

Severe pneumonia

[i]. Antibiotics Preferred
Co-amoxiclav 1.2g tds IV and doxycycline 200mg PO initially then 100mg od

Alternative

Levofloxacin 500mg od (preferably oral)

[ii]. Microbiological Investigations

Sputum culture
Culture the blood if septicaemic
Baseline CRP
Urine for antigen testing (pneumococcus and legionella)

[iii]. Oral switch

Early IV/oral switching is effective even in severe pneumonia and oral amoxycillin, co-amoxiclav, doxycycline and levofloxacin are all well orally absorbed

[iv]. Duration

Most community acquired pneumonias need no more than 5 days of antibiotics.

[b]. Hospital-acquired pneumonia

The aetiology of a pneumonia presenting greater than 96 hours after admission to hospital differs markedly from community acquired disease. Pathogens such as aerobic gram-negative rods are more frequently identified

Patients known as being MRSA colonised in the past (see PIMS alerts) should receive in addition to standard antibiotics, treatment for MRSA until it can be excluded (see section 4c)

Within five days of admission
Manage as for community acquired

Five or more days after admission

[i] Antibiotics Preferred

Piperacillin/tazobactam 4.5g tds IV

Alternative

Levofloxacin 500mg od (preferably oral)

[ii]. Microbiological Investigations

Sputum culture
Culture the blood if septicaemic
Baseline CRP

[iii]. Oral switch

There is no appropriate oral switch

[iv]. Duration

Most hospital acquired pneumonias need no more than 5 days of antibiotics.

[c]. MRSA pneumonia

MRSA is becoming an increasingly unusual infection at LSW. Specific therapy should be targeted at those patients most likely to benefit based on their risks for MRSA pneumonia eg.

- **Past history of MRSA colonisation as noted on PIMS**
- **Admission from Nursing or Residential Home**
- **Severe healthcare associated disease**

[d]. Necrotizing staphylococcal pneumonia

Respiratory tract infections with S. aureus strains that produce the Panton-Valentine leucocidin (PVL) can cause severe life threatening pneumonia. Locally most strains are flucloxacillin sensitive though worldwide MRSA-PVL are more common

Alert signs for necrotizing pneumonia include

- Multi-lobar infiltrates
- Clinically severe pneumonia especially in the young, in such patients the CURB-65 score may be low eg 0-1
- Haemoptysis and frank pulmonary haemorrhage
- Leucopenia
- Pleural effusions

If necrotising pneumonia is suspected contact the on call Microbiologist immediately

[i]. Antibiotics

Linezolid 600mg bd, rifampicin 600mg bd and clindamycin 1.2g qds IV. This triple combination should be used in all cases regardless of flucloxacillin susceptibility
If the diagnosis is suspected but not confirmed add additional beta lactam or quinolone antibiotics to cover for common causes of pneumonia.

[ii]. Microbiological Investigations

As for other pneumonias
A sputum or BAL sample is useful as in most cases the organism can be easily isolated from this site.
Contact the on call Microbiologist and request urgent gram stain of respiratory samples

[d]. Infective exacerbation of COPD

[i]. Antibiotics

Doxycycline 200mg PO loading followed by 100mg PO od

[ii]. Microbiological Investigations

Sputum culture
Culture the blood if septicaemic
Baseline CRP

[iii]. Duration

Most infectious exacerbations need no more than 5 days of antibiotics.

5. Soft Tissue Infections

Microbiological Investigations for all categories

Pus or debrided deep tissues (preferable) or wound swab
Aspiration of cellulitis has a low diagnostic yield and is painful
Culture the blood if septicaemic
Baseline CRP
Clotted blood for streptococcal antibodies in community acquired cellulitis

[a]. Post operative wound infections

The majority of postoperative wound infections are due to S. aureus of which many are MRSA.

i. Infection of a *clean* operative site

[i]. Antibiotics Preferred

Flucloxacillin 2g IV qds or 1g PO qds depending on severity

Alternative

If non severe allergic to penicillins and orals are suitable cephradine 1g qds (see Part 1 section 8 penicillin allergies) or clarithromycin 500mg bd

If known/suspected to be infected with MRSA treat mild non-bacteraemic infections with oral doxycycline 100mg bd and oral rifampicin 300mg bd or teicoplanin plus oral rifampicin if septic or previous MRSA isolates resistant to tetracyclines

Review need for teicoplanin at 48-72 hours and consider substituting for flucloxacillin if no evidence of MRSA infection

[ii]. Oral switch

Flucloxacillin 1g qds, clarithromycin 500mg bd or doxycycline 100mg bd and rifampicin 300mg bd depending on sensitivities.

If the use of linezolid (well absorbed and highly reliable anti gram positive activity) will expedite discharge contact the on call Microbiologist

[iii]. Duration

Most simple wound infections can be treated with 7 or fewer days of antibiotics

[b]. Infection of a clean-contaminated site eg operation crossed a mucosal surface

[i]. Antibiotics Preferred

Co-amoxiclav 1.2g IV tds. In case of suspected MRSA infection add suitable anti MRSA regimens as noted above

Alternative

Levofloxacin 500mg bd plus metronidazole (both preferably oral).
In case of suspected MRSA infection add suitable anti MRSA regimens as noted above

[ii]. Oral switch

Agents such as flucloxacillin, co-amoxiclav and doxycycline are suitable for oral switch therapy; selection depends on microbiological and clinical findings.
If the use of linezolid (well absorbed and highly reliable anti gram positive activity) will expedite discharge contact the on call Microbiologist.

[iii]. Duration

Most simple wound infections can be treated with 7 or fewer days of antibiotics

[c]. Cellulitis

Non-Facial

Cellulitis is an infection of the superficial layers of the skin. If associated with a wound infection see above. Cellulitis is usually due to S. aureus or streptococci

Preferred

Flucloxacillin 2g IV qds or 1g PO qds depending on severity

Alternative
If non severe allergy to penicillins and orals are suitable cephradine 1g qds (see

section 8 penicillin allergies) or clarithromycin 500mg bd

If known/suspected to be infected with MRSA treat mild non-bacteraemic infections with oral doxycycline 100mg bd and oral rifampicin 300mg bd or teicoplanin plus oral rifampicin if septic or previous MRSA isolates resistant to tetracyclines. In the event of a treatment failure bear in mind that many haemolytic streptococci are resistant to tetracyclines

Review need for teicoplanin at 48-72 hours and consider substituting for flucloxacillin if no evidence of MRSA infection

[ii]. Oral switch

Flucloxacillin 1g qds, clarithromycin 500mg bd or doxycycline 100mg bd and rifampicin 300mg bd depending on sensitivities.
If the use of linezolid (well absorbed and highly reliable anti gram positive activity) will expedite discharge contact the on call Microbiologist

[iii]. Duration

Most simple wound infections can be treated with 7 or fewer days of antibiotics

[d]. Facial cellulitis

Due to the proximity of the facial air spaces, anti-anaerobic and gram negative cover is required when empirically treating orbital and facial cellulitis. Benzylpenicillin, flucloxacillin and amoxycillin are options if cellulitis is confirmed as due to streptococci or staphylococci

[i]. Treatment

Co-amoxiclav 1.2 g tds IV or 625mg tds PO depending on severity

If known/suspected to be infected with MRSA for mild non-bacteraemic infections **add** oral doxycycline 100mg bd and oral rifampicin 300mg bd or teicoplanin plus oral rifampicin if septic or previous MRSA isolates resistant to tetracyclines.

[ii]. Oral switch

Agents such as flucloxacillin, co-amoxiclav and doxycycline are suitable for oral switch therapy. The choice of agent will depend on the cause of the infection and response to empirical treatment
If the use of linezolid (well absorbed and highly reliable anti gram positive activity) will expedite discharge contact the on call Microbiologist

[e]. Bites

Most bite wounds if promptly cleaned at the time of the injury do not require empirical antibiotics
Injuries at high risk of infection, which should be considered for prophylactic or pre-emptive treatment, include[9]**:**

- Crush and deep puncture (especially cat) bites
- Wounds to the hands, face and genitals
- Bites affecting the immunocompromised and asplenic/hyposplenic

Grossly contaminated bites should be treated with tetanus toxoid/ immunoglobulin as per local protocol

Antibiotics Preferred
Co-amoxiclav 1.2g tds IV or 625 mg tds PO

Alternative

Levofloxacin 500mg PO od and clindamycin 300mg PO qds
Erythromycin and clarithromycin are not appropriate antibiotics as they are ineffective against pasteurella sp

[iii]. Oral switch

See above

[iii]. Duration

Most bite infections can be treated with 7 or fewer days of antibiotics

[f]. Chronic and Diabetic Ulcers (see Diabetic Care pathway for further detail)

Ulcers that are not clinically infected need neither microbiological sampling nor treatment. Even a clean ulcer will yield bacteria on culture. Their presence does not necessarily indicate infection

Mild infection:	Superficial inflammation with no deep tissue involvement and no systemic signs of infection Treat as for a staphylococcal infection, see Infection of a *clean* operative site noted above
Moderate disease	Infection deep to the fascial layers, involving bone or spreading

	cellulitis/lymphangitis, co-amoxiclav 1.2g tds IV or levofloxacin 500mg bd (preferably oral) plus clindamycin 450mg qds PO (preferred) or 600mg tds IV If known/suspected to be infected with MRSA **add** empirical anti-MRSA treatment eg oral doxycycline 100mg bd and oral rifampicin 300mg bd or IV teicoplanin and oral rifampicin
Severe disease	For infections associated with systemic sepsis discuss with the on call Microbiologist

[ii]. Oral switch

In mild disease oral flucloxacillin 1g qds or clarithromycin 500mg bd are appropriate oral treatments. In moderate disease oral co-amoxiclav 625mg tds may be suitable
The combination of levofloxacin 500mg od and clindamycin 450mg qds is reserved for **specialist directed bone and deep tissue treatment**. This has a large potential to cause antibiotic associated/ C. difficile diarrhoea and should be discussed with the on call Microbiologist

[iii]. Duration

Most infections can be treated with 7 or fewer days of antibiotics

[g]. Necrotizing fasciitis (including Fournier's gangrene and other mixed culture severe skin and soft tissue infections)

Necrotizing fasciitis is a medical emergency necessitating extensive and rapid tissue debridement as well as antibiotics. The best investigation is surgical exploration

These necrotizing wound infections penetrate below the superficial fascial planes. Thrombosis of perforating vessels leads to extensive tissue damage that is present before obvious changes to the overlying skin. Clinical clues include**:**

- Systemic sepsis out of proportion to the clinical signs
- Pain that appears exaggerated or out of proportion
- Skin mottling and change in colour to a grey or violaceous hue
- Blistering of the skin
- Cutaneous anaesthesia

Until the diagnosis is confirmed or refuted meropenem 1g IV tds and clindamycin 1.2g qds IV
If identified as type 2 disease (streptococcal necrotizing fasciitis) a change to benzylpenicillin 2.4g every four hours plus clindamycin (as noted above) may be considered in consultation with a microbiologist

6. Intra abdominal infections[5]

Cephalosporins and quinolones are high risk antibiotics for Clostridium difficile disease and should be avoided wherever possible. For the vast majority or individuals co-amoxiclav is appropriate

A wide variety of pathogens can cause intra abdominal infections. Only broad guidance on the management of these infections is possible here. For further information contact the on call Microbiologist

Cephalosporins are to be avoided except in penicillin allergy (see Part 1 section 8) and when indicated the preferred agent is IV cefuroxime usually in combination with metronidazole

Microbiological Sampling

Pus (preferable) or wound swabs
Operative cultures of community perforations are often of little diagnostic significance whereas samples from complicated/hospital associated infections are of great benefit when excluding infection due to resistant microbes.
Fluids from longstanding drains should not be sampled opportunistically as differentiation of pathogen from coloniser is often impossible
Culture the blood if septicaemic
Baseline CRP

Metronidazole

Co-amoxiclav, piperacillin/tazobactam and meropenem/ertapenem have good activity against anaerobes. The concurrent use of metronidazole may be considered with co-amoxiclav where there is extensive soiling by the lower GI tract. Metronidazole rarely needs to be added to piperacillin/tazobactam or carbapenems

Metronidazole is well absorbed PO and this route should be used wherever possible

[1]. Intra abdominal collections, perforations and biliary tract infections

[a]. Community associated

[i]. Antibiotics Preferred

Co-amoxiclav 1.2g tds IV
Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use piperacillin/tazobactam or in the event of

past history of ESBL or admission from residential care, meropenem in the first instance

Alternative

Levofloxacin 500mg bd and metronidazole tds (both preferably oral)
Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use meropenem 1g tds IV providing no severe allergy to beta lactams (see part 1 section 8) otherwise contact the on call Microbiologist

Consider teicoplanin in those at risk of MRSA infection especially in the presence of severe sepsis

[b]. Hospital or healthcare associated (includes residential care, those with indwelling IV lines and frequent contact with in patient services)

[i]. Antibiotics Preferred

Piperacillin/tazobactam 4.5 g tds IV. Consider once daily gentamicin 5mg/kg in severe sepsis. If impaired renal function prevents the use of gentamicin use meropenem 1g tds IV.

Alternative

Levofloxacin 500mg bd, metronidazole tds (both preferably oral). Consider once daily gentamicin 5mg/kg in severe sepsis. Where impaired renal function prevents the use of gentamicin use meropenem 1g tds IV in place of levofloxacin providing no severe allergy to beta lactams (see part 1 section 6) otherwise contact the on call Microbiologist
In patients admitted with severe sepsis from residential care or previously infected with an ESBL bacterium consider replacing co-amoxiclav, piperacillin/tazobactam or levofloxacin and metronidazole with meropenem and discuss with on call Microbiologist

Consider teicoplanin in those at risk of MRSA infection especially in the presence of severe sepsis

[ii]. Oral switch

Direct switch from IV co-amoxiclav or IV levofloxacin and metronidazole to similar oral formulations, 625mg tds or 500mg bd respectively is appropriate

Where no similar oral option exists no switch may be possible. For further advice discuss with the on call Microbiologist

[iii]. Duration

For further advice discuss with the on call Microbiologist

[c] Recurrent peritonitis due to perforations

Review previous treatments and where extensively pre treated try to avoid previously used antibiotics. Consider whether additional fluconazole or caspofungin is indicated. If caspofungin is used discuss with the on call Microbiologist

7. Acute Gastroenteritis (excluding C difficile disease)

Most episodes of acute gastroenteritis are viral and even confirmed bacterial cases are usually self limiting. Antibiotic treatment should be reserved for confirmed cases of salmonella, shigella or campylobacter in certain patient groups. Acute bacterial gastroenteritis can be due to many bacteria with differing susceptibilities eg optimal treatment for campylobacter is clarithromycin but this has little effect on salmonella. Infections such as vero toxin producing E coli (VTEC) and C difficile may be exacerbated by antibiotics. A bacteriological diagnosis should be made before starting antibiotics in most cases unless clinically likely to be C difficile disease (see part 2 section 14)

Salmonella
Consider treatment in:

- Children under the age of 3 months
- Adults over the age of 50
- Overtly immunosupressed especially if infected with HIV
- Those with significant cardiac valvular or atheromatous plaque disease

Typical regimens include trimethoprim and levofloxacin 500mg od for 5 days

Shigella

Consider treatment of all cases of bacterial dysentery and certainly in all non S. sonnei cases

Typical regimens include trimethoprim and levofloxacin 500mg od for 3 days

Campylobacter

Consider treatment in those with high fever, bloody colitis (after exclusion of VT producing E coli), incapacitating abdominal pain, progressively worsening diarrhoea or

disease for >7 days

Typical regimens include oral clarithromycin or levofloxacin for 5 days. Up to 20% of all UK disease is due to quinolone resistant bacteria

Verotoxin producing E coli (VTEC/EHEC)

The commonest cause of VTEC in the UK is serotype 0157 E coli but there are many other strains that local hospital laboratories are unable to identify. In the event of identifying a patient with unexplained bloody diarrhoea or haemolytic uraemic syndrome contact the on call Microbiology to request further stool testing. Unless there is an alternative life threatening infection avoid all antibiotics as these may exacerbate the condition

Discussion of other causes of gastroenteritis is outside the scope of this guideline. For further advice contact the on call Microbiologist

8. Septic Arthritis

Native Joint
The majority of community acquired septic arthritis is due to S. aureus. In the elderly and immunocompromised coliforms are increasingly implicated. It is vital that appropriate aspirates are taken to confirm the diagnosis and exclude crystal arthropathies. If a septic arthritis is confirmed, discuss with on call orthopaedics regarding joint washout[10]

[i]. Antibiotics Preferred

Flucloxacillin 2g qds IV plus gentamicin (review at 24 hours) or flucloxacillin plus oral rifampicin 300mg bd if known to be due to staphylococcus.

Alternative

Clindamycin IV 600mg tds IV plus gentamicin (review at 24 hours) or oral rifampicin 300mg bd if known to be due to staphylococcus.

If known/suspected to be infected with MRSA replace the selected gram positive agent (flucloxacillin or clindamycin) with IV teicoplanin plus rifampicin

Review need for teicoplanin at 48-72 hours and consider substituting for flucloxacillin if no evidence of MRSA infection

Discussed treatment plan with a Microbiologist once cultures available. Long-term

gentamicin treatment is NOT appropriate for septic arthritis as there are less toxic alternatives

[ii]. Microbiological Sampling

Joint aspirate (before starting antibiotics)
Culture the blood if septicaemic
Baseline CRP

[iii]. Duration and oral treatment

Septic arthritis is typically treated for 4-6 weeks. As a rule of thumb the first 1-2 weeks should be IV with an oral switch when evidence of clinical improvement. If a levofloxacin and rifampicin regimen is suitable then a shorter IV course may be possible. For further advice discuss with a microbiologist.

Prosthetic Joint Arthritis

Do not use empirical antibiotics without first discussing the case with a microbiologist or Orthopaedic surgeon

9. Osteomyelitis

Issues surrounding the management of Osteomyelitis are complex and not included in this generic document. If further advice is required contact a microbiologist. For further information regarding spinal osteomyelitis and epidural abscess refer to Neurosurgical Antibiotic Therapy Guidelines for Adult Patients PHNT.

10. Genital tract infections[11]

Sexually transmitted infections tend to be transmitted together so presence of one infection should raise suspicions of other infections. On diagnosis of an STI discuss further management and contact tracing with a microbiologist or GUMed Physician

[a]. Urethritis

The common infective causes of urethritis are Chlamydia trachomatis, Herpes simplex and Neisseria gonorrhoea. Wherever possible infection should be confirmed though this should not prevent empirical treatment if infection is likely.

[i]. Antibiotics

Chlamydia urethritis/cervicitis
Preferred
Azithromycin 1g single dose

Alternative
Doxycycline 100mg bd PO for one week

Gonococcal urethritis/cervicitis
Preferred

Ceftriaxone 500mg IM single dose

Alternative

Cefixime PO 400mg single dose. This is as effective as IM ceftriaxone for anogenital disease but less so for pharyngeal infections
Contact the on call Microbiologist in the event of allergy to cephalosporins or severe allergy to penicillins (see part 1 section 8)

Unless either Chlamydia or gonorrhoea can be excluded treatment of both is usually indicated

[ii]. Microbiological Sampling

Per urethral/endocervical swab in charcoal transport medium, for bacterial culture
Per urethral/endocervical swab in a universal transport medium swab for Chlamydia and herpes PCR
Blood cultures if suspect disseminated gonococcal infection

[b]. Conditions associated with vaginal discharge

Infections such as cervicitis and extensive herpes can present predominantly with vaginal discharge. Cervical examination is often able to identify these

Bacterial vaginosis

This is due to abnormal vaginal flora

[i]. Microbiological Sampling

Microbiological confirmation not required unless pregnant or refractory to treatment
High vaginal swab for clue cell microscopy

[ii]. Treatment

Metronidazole 400mg tds PO for one week
Alternative is single dose 2g metronidazole PO. This should be avoided in pregnancy
Alternative topical therapies are available. If indicated contact a microbiologist

Trichomonal vaginitis

This is an unusual sexually transmitted infection in the UK. The typical signs are those of a frothy greenish discharge

[i]. Microbiological Sampling

High vaginal swab, request specific microscopy for TV

[ii].Treatment

Single dose 2g metronidazole PO, this should be avoided in pregnancy.
Metronidazole 400mg tds PO for one week

[c] Pelvic Inflammatory Disease

PID is an ascending infection of the female genital tract and involves the endometrium and oviducts (salpingitis)

[i]. Antibiotics Preferred
Co-amoxiclav 1.2 g tds IV plus doxycycline 100mg bd PO

Alternative
Doxycycline 100mg bd PO plus metronidazole 400mg tds PO
Oral or IV levofloxacin 500mg od plus metronidazole 400mg tds PO

There is no published evidence to gauge the effectiveness of oral cephalosporins and these should be avoided in the treatment of PID

It is important that gonorrhoea is excluded in all cases using urethral and cervical cultures as the advised regimens are not ideal for some strains of gonococcus. If GC cannot be excluded consider adding a single IM dose of ceftriaxone

[ii]. Microbiological Sampling

As for cervicitis/urethritis
Pus (preferable) or swab of intrabdominal pus
Blood cultures if suspect disseminated gonococcal infection

[iii] Oral switch

In severe disease (especially if tubo-ovarian abscess) initial treatment should be parenteral. In most cases oral switch at 24-48 hours is appropriate

[iii]. Duration

14 days of all antibiotics

11. Antibiotic prophylaxis, treatment and vaccination in hyposplenism

See guidelines on Trustnet

12. Treatment of Meticillin resistant infections[12]

MRSA are by definition resistant to all beta lactam antibiotics available at LSW. They are usually resistant to quinolones and over half are resistant to erythromycin, clarithromycin and clindamycin. There are many other useful antibiotics available for treatment other than teicoplanin

Treatment of confirmed MRSA infections

Over 90% of local MRSA strains are sensitive to glycopeptides (vancomycin and teicoplanin), trimethoprim, gentamicin, doxycycline, rifampicin and fusidic acid. The latter two agents must not be used as monotherapy. The following options are suitable for most strains though the prescriber must review available sensitivities.
Septicaemia/bacteraemia Treatment options include teicoplanin plus oral rifampicin, daptomycin, and linezolid and will be directed by a Microbiologist

UTI	Trimethoprim 200mg bd PO Nitrofurantion 100mg modified release bd for uncomplicated UTI (avoid in those with complicated urinary tract including in dwelling catheters) Doxycycline 100mg od PO

Skin and soft tissue	Clarithromycin 500mg bd PO if sensitive or doxycycline 100mg bd PO and rifampicin 300mg bd PO if mild non bacteraemic disease
Bone and joint infection	Teicoplanin and oral rifampicin. If sensitive consider oral clindamycin. Clindamycin is associated with C. difficile infection and care should be taken when using in the elderly.
Respiratory tract infection	Linezolid (preferably oral) 600mg bd OR oral doxycycline 100mg od PO and oral rifampicin 300mg bd PO depending on severity. Doxycycline and rifampicin are a linezolid sparing regimen suitable for non severe disease

13. Endocarditis- Treatment and Prophylaxis

See guidelines on Trustnet

14. Clostridium difficile associated disease[13]

Clostridium difficile colitis is usually secondary to antibiotic use. Other precipitators include abdominal surgery and chemotherapeutic agents

The mainstay of treatment is withdrawal where safe of inciting antibiotics. In most cases treatment with a specific anti-clostridial agent is appropriate. In severe disease early empirical treatment can be life saving

Algorithim 1 *C. difficile* associated disease

Primary episode and first reoccurrence

Withdraw inciting event/antibiotic if possible

Isolate patient

Non-severe disease

Oral metronidazole 400mg tds for 10 days

IV metronidazole 500mg tds for 10 days if nil by mouth

Severe disease

Any of:

- White cell count >15x10^9/l
- Acutely deteriorating renal function eg serum creatinine>1.5 times the pre morbid level

Algorithim 2

***C. difficile* associated disease**
From second reoccurrence onwards

Withdraw inciting event/antibiotic if possible

Stop PPI if safe to do so

Oral vancomycin 125mg qds PO 14 days CONSULT with on call Microbiologist as oral vancomycin is a restricted antibiotic (Δ)

Complete 10 days of treatment

The risk of relapse is up to 25% and in the event of the first reoccurence repeat this algorithm. See below for further relapses. There is no evidence that earlier conversion to oral vancomycin in non-severe disease leads to a more rapid cure

improvement

Diarrhoea persisting after 14 days of oral metronidazole

Especially if any of:
White cell count >15x10^9/l
Acutely deteriorating

ect resolution of diarrhoea within 1-2 weeks

solve or there are further relapses discuss further therapeutic options with the on call Microbiologist

restricted antibiotic (Δ)

the on call Microbiologist and Gastroenterologist

Daily review

If the patient deteriorates moving to severe disease consider switching to oral vancomycin

Severe CDAD must be managed with in put from Microbiology, Gastroenterology, Surgery and Critical care. In the event of a deteriorating situation especially where the patient is unable to tolerate oral antibiotics or signs of an acute abdomen urgent assistance is indicated to consider the suitability for alternative drug delivery routes and surgical intervention

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All policies are required to be electronically signed by the Lead Director (the policy will not be accepted onto Healthnet until the e-signature is received). The proof of signature for all policies is stored in the policies database.

The Lead Director approves this document and any attached appendices.

Signed:

Title:

Date: