University Hospitals of Derby and Burton NHS Foundation Trust

# Leg Ulcer Infection in Adults - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/2024/076

## Introduction

- According to NICE (2020) a leg ulcer is a “long-lasting (chronic) open wound that takes more than 4 to 6 weeks to heal”. Leg ulcers usually develop on the lower leg, between the shin and the ankle.

- There are many causes of leg ulcers, and although most leg ulcers are colonised by bacteria, few are actually infected. Antibiotics do not promote healing when a leg ulcer is not clinically infected

- The most common causative organisms in leg ulcer infections are Gram positives such as *Staphylococcus aureus* and beta-haemolytic *Streptococci spp*.

- Risk factors for infected leg ulcers include diabetes, venous insufficiency, arterial disease and immunosuppression. Underlying conditions such as venous insufficiency and oedema should be managed appropriately to promote healing

- Some common signs of infection (localised redness, discharge or an unpleasant odour) may be present in all leg ulcers irrespective of infection status, particularly if compression is removed. Therefore, clinicians should assess for the following signs to determine if the ulcer is infected:
    - Redness or swelling spreading beyond the ulcer itself
    - Localised heat
    - Increased pain
    - Fever

- Temperatures > 38 ° C or < 36 ° C, respiratory rate > 20 breaths/minute, heart rate > 90 beats/minute, and hypotension can denote progression of localised infectious disease into sepsis and septic shock.

Please note that this guideline does not cover the following conditions:

- Erysipelas & Cellulitis
- Cellulitis associated with Human Bites and Animal Bites
- Soft tissue infection associated with water exposure
- Surgical site infections
- Lacerations
- Diabetic foot infection
- Necrotising soft tissue infections

Refer to the appropriate guideline on NETi for the above conditions

This guideline should also be read in conjunction with the UHDB Leg Ulcer Guideline and the First Line Wound Management Guidance for Infected Leg Ulcers for advice and guidance on wound management.

## Investigation

Symptoms and signs provide the criteria for the diagnosis of infected leg ulcers. The investigations outlined herein provide guidance for treatment, rather than diagnostic criteria.

### Examination

- All patients admitted to UHDB with a leg ulcer should have a Holistic assessment of the wound(s) completed on admission (or at the earliest opportunity). This includes:
    - Wound photography - photography/mapping is advised at regular intervals, this allows for progress (or deterioration) to be monitored and action taken as required.
    - Wound mapping if photography not available
    - Wound Dimensions
    - Condition of surrounding skin
    - Wound swab - see "Microbiology" below
- If the ulcer is long-standing, consider the possibility of osteomyelitis and investigate appropriately

### Microbiology

- ± Blood cultures:
    - Bacteraemia is relatively uncommon in infected leg ulcers. However, culture and resistance/susceptibility profiles enable de-escalation and optimisation of antimicrobial chemotherapy. Blood cultures are recommended with:
        - Episode(s) of fever; or
        - If the differential diagnosis includes bloodstream infection, sepsis, or septic shock; or
        - If for initiation of treatment with intravenous antibiotics.
- MRSA screen:
    - *Staphylococcus aureus* is a common cause of infection in leg ulcers. Therefore, an MRSA screen is recommended.
- ± aspirate, wound swab or loose tissue for culture, if clinical signs of infection and if obtainable.
    - Note that chronic leg ulcers will naturally be colonised and will be positive even in the absence of infection, bear this in mind when deciding whether to treat with antibiotics

### Blood sciences

- Full blood count (FBC), C-reactive protein (CRP), ± lactate, urea and electrolytes (U&Es), and liver function tests (LFTs)

## Treatment

### Intravenous versus per oral antibiotics; community versus hospital

- Criteria for intravenous:
    - (1) Proximity of ulcer and associated cellulitis to medical device (e.g. prosthetic joint).
    - (2) Progression of symptoms and signs after 48 hours of per oral antibiotics.
    - (3) Suboptimal vasculature - e.g. chronic venous insufficiency, diabetes mellitus, peripheral vascular disease - impeding delivery of antibiotics.
    - (4) Intolerant of per oral antibiotics.
    - (5) Sepsis.
    - (6) Septic shock.

### Empiric antibiotics

Review the past microbiology results, with specific reference to previous soft tissue samples.

The most common causative organisms in leg ulcer infections are Gram positives such as *Staphylococcus aureus* and beta-haemolytic *Streptococci spp*.

In patients with chronic ulcers and multiple co-morbidities (e.g. diabetes, immunocompromised, vasculopathy, post-surgery, retention of metal work), infection may also be caused by Gram negative and anaerobic bacteria therefore this must be taken into consideration when prescribing antimicrobial treatment.

If Gram negative organisms, including multi-drug resistant organisms such as ESBL/AMPc producers or CRE/CRO are isolated from a post-antibiotic sample, interpret the results carefully as these microbes may represent colonisation at this site and are not necessarily an indication for antibiotics. If the patient is symptomatic and if clinically indicated, an appropriate antibiotic may be selected from the sensitivity profile reported on the relevant EPMA system.

If a multi-drug resistant organism is isolated, ensure appropriate infection control precautions are adhered to when caring for the patient

### Antibiotics are only indicated for leg ulcers:

1) Where an organism(s) is isolated AND when the patient presents with systemic symptoms of infection (pyrexia, rigors, tachycardia etc.)

    OR

2) For patients presenting with any of the following:
    - redness or swelling of the skin spreading beyond the ulcer itself
    - delayed healing
    - unexpected/disproportionate pain
    - abnormal odour
    - pocketing at the base of the wound
    - discoloured (i.e. unusually dark) granulation tissue
    - friable granulation tissue
    - devitalised (sloughy or necrotic) tissue.

**Note regarding penicillin allergies**

Please note that in the context of this guideline, "penicillin allergy" refers to both "non-severe penicillin allergy" i.e. non-immediate without systemic involvement and "severe penicillin allergy" i.e. immediate rapidly evolving or non-immediate with systemic involvement

## Empiric, per oral antibiotics

| | |
|---|---|
| **First Line** | Flucloxacillin 500mg to 1g PO QDS |
| **Second line** (penicillin allergy or likely/known MRSA) | Doxycycline* 100mg PO BD |
| **Alternative second line** if pregnant | Erythromycin 500mg PO QDS |
| **Third line** (penicillin allergy, intolerant to doxycycline) | Clarithromycin 500mg PO BD |
| **If patient has a history of diabetes or arterial disease, or other risk factors for anaerobic infection** | +/- Metronidazole 400mg PO TDS (in addition to the above regimes) |

*NB Doxycycline is contraindicated in pregnancy; if likely/known MRSA, discuss with microbiology for pregnant patients

## Empiric, per oral antibiotics, failure to respond to first line options, systemically well

| | |
|---|---|
| **First Line** | Co-Amoxiclav 625mg PO TDS |
| **Second line** (penicillin allergy) | Co-Trimoxazole** 960mg PO BD<br><br>**PLUS** if history of diabetes or arterial disease or other risk factors for anaerobic infection:<br>Metronidazole 400mg PO TDS |
| **Alternative second line** in pregnancy | Discuss with microbiology |
| **Likely or confirmed MRSA** | Linezolid*** 600mg PO BD<br><br>**PLUS** if history of diabetes or arterial disease or other risk factors for anaerobic infection:<br>Metronidazole 400mg PO TDS |
| **If there is no response to empiric per oral antibiotics but the patient is systemically well, discuss with Microbiology** | |

**NB Co-trimoxazole is contraindicated in pregnancy

*** Linezolid has multiple contraindications and interactions that must be considered before prescribing should occur; furthermore, there are mandatory monitoring requirements that must be performed during therapy e.g. weekly blood monitoring; consult the BNF or discuss with a pharmacist.

## Empiric, intravenous antibiotics, concerns over enteral absorption, failure to respond to empiric per oral antibiotics and/or systemically unwell (not sepsis)

| | |
|---|---|
| **First Line** | Flucloxacillin 2g IV 6 hourly |
| **Second line** (penicillin allergy, likely/known MRSA and/or pregnancy) | Vancomycin IV, dosed as per hospital guidelines (target level 10-15mg/L) |
| **If patient has a history of diabetes or arterial disease, or other risk factors for anaerobic infection** | +/- Metronidazole 500mg IV TDS (in addition to the above regimes) |

## Empiric, intravenous antibiotics, systemically unwell including red flag sepsis

- This antibiotic section includes fluoroquinolone usage.
- The Medicines and Healthcare products Regulatory Agency (MHRA) - with input from the Commission on Human Medicines (CHM) - have reviewed and published drug safety updates regarding systemic fluoroquinolones.
- Ciprofloxacin is hyperlinked to the British National Formulary.
- For NHS medicines and MHRA information for healthcare professionals on ciprofloxacin, click here and here, respectively.
- For MHRA printable information for patients on fluoroquinolones, click here.

| | |
|---|---|
| **First Line** | Piperacillin/Tazobactam 4.5g IV TDS (increased to QDS if concerns regarding *Pseudomonas aeruginosa*)<br><br>**PLUS** If likely/known MRSA:<br>Vancomycin IV, dosed as per hospital guidelines (target level 10-15mg/L)<br>or<br>Teicoplanin IV, dosed as per hospital guidelines (target level 15-30mg/L) |
| **Second line** (penicillin allergy, non-pregnant) | Vancomycin IV, dosed as per hospital guidelines (target level 10-15mg/L)<br>or<br>Teicoplanin IV, dosed as per hospital guidelines (target level 15-30mg/L)<br>**PLUS**<br>Ciprofloxacin 400mg IV BD (increased to TDS if concerns regarding *Pseudomonas aeruginosa*)<br><br>**PLUS**<br>Metronidazole 500mg IV TDS |
| **Alternative second line** (penicillin allergy in pregnancy or where fluoroquinolones, e.g. Ciprofloxacin, are contraindicated) | Vancomycin IV, dosed as per hospital guidelines (target level 10-15mg/L)<br><br>**PLUS**<br>Aztreonam 1g IV TDS (increased to 2g QDS if concerns regarding *Pseudomonas aeruginosa*)<br><br>**PLUS**<br>Metronidazole 500mg IV TDS |

Please note, aztreonam supplies are stocked in pharmacy. Therefore:

- Liaise with pharmacy/pharmacist on call regarding the aztreonam prescription; and
- Administer the other antibiotics before the aztreonam is supplied; and
- Administer the aztreonam as soon as possible.

## Directed Therapy

For directed oral and intravenous antibiotic choices or OPAT options, refer to culture & sensitivity results on the relevant EPMA system or discuss with Microbiology

## Intravenous to per oral step down

- After 48 hours of intravenous antibiotics, if the patient is afebrile, observations stable, and inflammatory markers downward trending, collaborate with the senior(s) regarding per oral step down. Refer to the "Start Smart then Focus" Tool on the Antimicrobial Guidelines Page on Koha.

### Duration of antibiotics

- 7 days of treatment (combination of IV and PO routes) should usually be sufficient to effectively treat and infected leg ulcer

- Be aware that full resolution of the ulcer will not be expected at the time of antibiotic course completion and that it can take some time for it to visibly improve

- Longer durations (up to 14 days) may be required if the infection is not improving adequately, particularly in patients with poor healing and a higher risk of complications due to comorbidities

## Document control

| | |
|---|---|
| **Development of guidelines:** | Ellie Birnie (Lead Antimicrobial Pharmacist) |
| **Consultation with:** | Dr Chris Durojaiye (Infectious Diseases/OPAT Consultant)<br>Paul Hardy (Lead Tissue Viability Nurse Specialist)<br>Dr Adam Ferguson (Consultant Dermatologist)<br>Dr Tanya Bleiker (Consultant Dermatologist) |
| **Version:** | 2 |
| **Approval date:** | Medicine 12/08/2024<br>AMSG 27/08/2024 |
| **Changes from previous version:** | Introduction: reworded (minor) and reformatted (minor). Investigation: reworded (minor) and reformatted (minor). Treatment: addition of penicillin allergy wording as per NICE (minor), reworded (minor), reformatted (major). References: expanded (minor). |
| **Date uploaded:** | 28/08/2024 |
| **Next review date:** | August 2027 |
| **Key contacts:** | Ellie Birnie ellie.birnie1@nhs.net<br>Lead Antimicrobial Pharmacist |

## References

National Institute for Health and Care Excellence (NICE), 2020. NG152 Leg ulcer infection: antimicrobial prescribing. Available at www.nice.org.uk/guidance/ng152 (accessed 02/07/2024)

Basic Principles of Wound Management D. Armstrong & A. Meyr, June 2022

O'Meara et al, 2014. Antibiotics and antiseptics for venous leg ulcers. Cochrane Database of systematic reviews. Full text available online at https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003557.pub5/full (accessed 02/07/2024)

www.uptodate.com Evaluation and management of chronic venous insufficiency including venous leg ulcer (accessed 02/07/2024)

National Institute for Health and Care Excellence (NICE), 2019. NG141 Cellulitis and Erysipelas: antimicrobial prescribing. Available at Overview | Cellulitis and erysipelas: antimicrobial prescribing | Guidance | NICE (accessed 02/07/2024)

H. Boucher, 2020. Ulcerated Skin: Venous, Arterial Insufficiency, Pressure Decubuti. Sanford Guide. (Accessed 02/07/2024)

EUCAST clinical breakpoints and antibiotic dosing (V14.0, January 2024). (Accessed 02/07/2024)

Practice Guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America. Clinical Infectious Diseases 2014;59:e10-52.