Guideline for the Antibiotic Management of Diabetes Related Foot Infections in Adults

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V6	November 2023	Caroline Hallam	Update required. Changes to antibiotic section Removal of QEHKL as no longer a joint guideline

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Joint Guideline for the Antibiotic Management of Diabetes Related Foot Infections in Adults	18th January 2024

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:

During its development it has been circulated for comment to the endocrinology and vascular clinical governance leads, the podiatrists and the Foot MDT.
Comments were addressed and incorporated if appropriate

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to the NNUH. please refer to local Trust's procedural documents for further guidance.

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Joint Trust Guideline for the Antibiotic Management of Diabetes Related Foot Infections in Adults

Quick Reference Guideline

Table 1: Stages of Infection of Diabetes Related Foot Infection

Clinical Description	Degree of infection
No purulence or evidence of inflammation	**Uninfected**
Evidence of inflammation 2cm or less around the ulcer	**Mild**
Cellulitis >2cm around the ulcer	**Moderate**
Cellulitis >2cm around the ulcer associated with; • Lymphangitis • Foot failing to respond to oral antibiotics alone	**Severe – Borderline admission**
Cellulitis as well as evidence of systemic toxicity; • Fever • Hypotension • Leukocytosis or • Abscess formation • Infection tracking beneath fascia • Foot not responding to antibiotics • Wet gangrene	**Severe - Admission**
Visible bone in wound or where there is a positive 'probe to bone' test with an overlying wound, or if there are X-ray changes consistent with osteomyelitis	**Osteomyelitis**

Table 2: Empiric Treatment for Diabetic Foot Infection

Table 2:	First choice treatment	Second choice treatment or alternatives (e.g. if penicillin allergic patient)	At high risk of MRSA or MRSA positive	Duration	Comments
Mild	Flucloxacillin PO 500mg -1g qds	**1st line**: Doxycycline PO 200mg STAT Day 1 then 100mg bd **2nd line**: Cotrimoxazole PO 960 mg bd (contra-indicated if patient on methotrexate or has trimethoprim allergy) OR **3rd line:** Clarithromycin PO 500mg bd	**Prescribe according to sensitivities.** Doxycycline PO 200mg STAT Day 1 then 100mg bd **OR** Cotrimoxazole PO 960 mg bd (contra-indicated if patient on methotrexate or has trimethoprim allergy) **OR** Combination of 2 of the following oral antibiotics Trimethoprim po 200mg bd, rifampicin po 300mg-600mg bd, Fusidic acid po 500mg tds. (Fusidic acid not to be used in combination with rifampicin).	Review at 1-2 weeks	**Cotrimoxazole**: unlicensed in diabetic foot. Monitoring: 2 weekly FBC and U's and E's. See information sheet **Sodium fusidate monitoring**: See notes at bottom of table
Moderate	Co-amoxiclav PO 625mg tds	**1st line:** Cotrimoxazole PO 960 bd (contra-indicated if patient on methotrexate or has trimethoprim allergy)	**Prescribe according to sensitivities.**	2-4 weeks	**Cotrimoxazole**: unlicensed in diabetic foot. Monitoring: 2 weekly FBC and U's and E's See information sheet

		2nd line: Clindamycin PO 300mg-450mg qds (consider adding in Ciprofloxacin* 500mg PO bd if no improvement after 1-2 weeks)	**1st line:** Cotrimoxazole PO 960mg bd (contra-indicated if patient on methotrexate or has trimethoprim allergy) **2nd line** Doxycycline PO 200mg STAT Day 1 then 100mg bd Clindamycin PO 300mg-450mg qds		***Ciprofloxacin:** See important safety information in BNF on quinolones before prescribing. Counsel pt on side effects and ensure patient information leaflet is given. FQ-patient-sheet-final.pdf(publishing.service.gov.uk) Document in medical notes that a conversation has taken place regarding risks and benefits of using ciprofloxacin
Table 2:cont.	**First choice treatment**	**Second choice treatment Or alternatives (e.g. if penicillin allergic patient)**	**At high risk of MRSA or MRSA positive**	**Duration**	**Comments**

Severe Borderline Admission (this regimen will be reviewed regularly as to whether admission is necessary)	Ceftriaxone 2g od IV **AND** Ciprofloxacin* PO 500mg bd **AND** Metronidazole PO 400mg tds	**Penicillin Allergy** *(NOT anaphylaxis or urticarial response to penicillin)* Ceftriaxone 2g od IV **AND** Ciprofloxacin* PO 500mg bd **AND** Metronidazole PO 400mg tds **In Severe Penicillin Allergy** *(history of anaphylaxis or urticaria occurring immediately after penicillin therapy) or if MRSA positive use* Ciprofloxacin* PO 500mg bd **AND** Metronidazole PO 400mg tds **AND** Teicoplanin IV 800mg loading dose in clinic then if <70kg 400mg od OR if ≥70kg 6mg/kg od	**Penicillin Allergy or if MRSA positive use** Ciprofloxacin* PO 500mg bd **AND** Metronidazole PO 400mg tds **AND** Teicoplanin IV 800mg loading dose in clinic then if <70kg 400mg od OR if ≥70kg 6mg/kg od	Review in <1 week Usual max 2 weeks in this category	**PLEASE CONSIDER OPAT** Consider using Ciprofloxacin* PO 750mg bd if evidence of bone involvement ***Ciprofloxacin:** See important safety information in BNF on quinolones before prescribing. Counsel pt on side effects and ensure patient information leaflet is given. FQ-patient-sheet-final.pdf(publishing.service.gov.uk) Document in medical notes that a conversation has taken place regarding risks and benefits of using ciprofloxacin
Severe requiring admission	Piperacillin/Tazobactam IV 4.5g tds (qds may be used on advice of a consultant Microbiologist)	Vancomycin IV (dose as per vancomycin policy) **AND** Metronidazole PO 400mg tds (only use IV if oral route not available) **AND**	Piperacillin/Tazobactam IV 4.5g tds (qds may be used on advice of a consultant Microbiologist) + Vancomycin IV (dose as per vancomycin policy)	Regular review on diabetic foot round. IVs usually for 5-7 days after which review whether to step down to oral. Initial treatment duration usually 2-4 weeks (IV and oral course together)	Oral treatment should be guided by microbiology results, if none available consider Co-amoxiclav PO 625mg tds **OR** In penicillin allergy, Ciprofloxacin* PO 500mg bd **AND** Clindamycin PO 450mg qds ***Ciprofloxacin:** See important safety

		Ciprofloxacin* PO 500mg bd	Vancomycin IV (dose as per vancomycin policy) **AND** Metronidazole PO 400mg tds (only use IV if oral route not available) **AND** Ciprofloxacin* PO 500mg bd	If evidence of infection has not resolved after 4 weeks of apparently appropriate treatment, re-evaluate the patient and reconsider the need for further diagnostic studies or alternative treatment	information in BNF on quinolones before prescribing. Counsel pt on side effects and ensure patient information leaflet is given. FQ-patient-sheet-final.pdf (publishing.service.gov.uk) Document in medical notes that a conversation has taken place regarding risks and benefits of using ciprofloxacin
Table 2:cont.	**First choice treatment**	**Second choice treatment Or alternatives (e.g. if penicillin allergic patient)**	**At high risk of MRSA or MRSA positive**	**Duration**	**Comments**
Osteomyelitis Inpatient Treatment	Piperacillin/Tazobactam IV 4.5g tds (qds may be used on advice of a consultant Microbiologist)	Vancomycin IV (dose as per vancomycin policy) **AND** Ciprofloxacin* PO 750mg bd **AND** Metronidazole PO 400mg tds (only use IV if oral route not available) If patient to be discharged on OPAT switch Vancomycin to Teicoplanin prior to discharge. Teicoplanin IV 10mg/kg every 12 hours for 3 doses then 10mg/kg IV od (round dose to highest 100mg). Use actual body weight .	Piperacillin/Tazobactam IV 4.5g tds (qds may be used on advice of a consultant Microbiologist) **AND** Vancomycin IV (dose as per vancomycin policy) In penicillin allergy use treatment option in 2nd choice column If patient to be discharged on OPAT switch Vancomycin to Teicoplanin prior to discharge. Teicoplanin IV 10mg/kg every 12 hours for 3 doses then 10mg/kg IV od (round dose to highest 100mg). Use actual body weight	Total therapy usually 4-6 weeks, minimum of 2 weeks of IV antibiotics usually required. Oral depending on progress, ask microbiology advice	**PLEASE CONSIDER OPAT** **Monitoring:** Weekly LFTs, serum Cr, CRP, ESR and WBC **Teicoplanin levels.** Target trough level at 3-5 days, then once a week during maintenance Therapeutic Range: 20mg/L-60mg/L Consider a duration of up to 3 weeks of antibiotic therapy after minor amputation for diabetes related osteomyelitis of the foot and positive bone margin culture and 6 weeks for diabetes-related osteomyelitis without bone resection or amputation ***Ciprofloxacin:** See important safety information in BNF on quinolones before prescribing. Counsel pt on side effects and ensure patient information

					leaflet is given. FQ-patient-sheet-final.pdf (publishing.service.gov.uk) Document in medical notes that a conversation has taken place regarding risks and benefits of using ciprofloxacin

Table 2:cont.	First choice treatment	Second choice treatment Or alternatives (e.g. if penicillin allergic patient)	At high risk of MRSA or MRSA positive	Duration	Comments
Osteomyelitis outpatient	Co-amoxiclav PO 625mg tds If no evidence of healing after 2-4 weeks review culture and sensitivities and substitute with sodium fusidate + a second agent which organism known to be sensitive to.	Clindamycin PO 450mg qds Consider stopping Clindamycin and switching to Ciprofloxacin* PO 750mg bd **AND** Metronidazole PO 400mg tds if a gram negative organism identified or no evidence of improvement after 4 weeks	**Prescribe according to sensitivities.** Doxycycline PO 200mg STAT then 100mg bd **OR** combination of 2 of the following oral antibiotics trimethoprim po 200mg bd, rifampicin po 600mg bd, fusidic acid po 500mg tds. (Fusidic acid not to be used in combination with rifampicin).	6 weeks – 3 months	**Sodium fusidate** may cause an elevation of liver function tests (LFTs). Perform LFTs at baseline and then every 2 weeks during treatment for the first month. After this time according to clinical judgement – minimum requirement is every 4 weeks throughout treatment ***Ciprofloxacin:** see important safety information in BNF before prescribing. Ensure pt is counselled and PIL given FQ-patient-sheet-final.pdf (publishing.service.gov.uk)
OPAT (link to trust guideline, OPAT bone and joint)	Ceftriaxone 2g od IV **AND** Ciprofloxacin* PO 750mg bd (add if pseudomonas suspected) **AND** Metronidazole PO 400mg tds (add if anaerobes suspected) **OR** Teicoplanin IV 10mg/kg every 12 hours for 3 doses then 10mg/kg IV od (round dose to highest 100mg) **AND** If gram negative suspected add Ciprofloxacin* PO 750 mg bd If anaerobe suspected add Metronidazole PO 400mg tds				**Monitoring:** Weekly LFTs, serum Creatinine, CRP, ESR and WBC **Teicoplanin levels**. Target trough level at 3-5 days, then once a week during maintenance Therapeutic Range: >20mg/L-60mg/L ***Ciprofloxacin:** see important safety information in BNF before prescribing. Ensure pt is counselled and PIL given FQ-patient-sheet-final.pdf (publishing.service.gov.uk)

Notes:

- IM antibiotics should only be given where there are appropriate facilities available to treat anaphylaxis. Ceftriaxone 2g IM should be given as two separate 1g injections in different sites.
- Co-amoxiclav may cause cholestatic jaundice if use is prolonged, especially in patients over 65 years. If treatment continues over 2 weeks liver function tests (LFTs) should be carried out fortnightly for the first month and then monthly from then on for the duration of treatment.
- Cholestatic jaundice may occur up to 6 weeks after treatment is stopped.
- If macrolide resistant the organism is likely to be resistant to clindamycin unless sensitivities show otherwise. Sodium fusidate may cause an elevation of liver function tests (LFTs). Perform LFTs at baseline and then every 2 weeks during treatment for the first month. After this time according to clinical judgement – minimum requirement is every 4 weeks throughout treatment

Quick Reference Guide - Co-trimoxazole Information Sheet: For use by prescribers in the Diabetic Foot Clinic

This sheet is to be used as a guide to prescribing co-trimoxazole and is not exhaustive. For further information consult the BNF.

Indications:
Co-trimoxazole PO 960mg bd as a 2nd line treatment in patients with mild to moderate diabetic foot infection according to policy.

Contra-indications

- Co-trimoxazole should not be given to patients with a history of hypersensitivity to sulphonamides, trimethoprim, co-trimoxazole or any excipients of Co-trimoxazole
- Patient on methotrexate
- Severe liver disease
- Reduce dose by 50% if eGFR 15mL/minute to 30mL/ minute, if eGFR <15 avoid or discuss with pharmacy
- Patients with acute porphyria

Cautions

- Patients with asthma or severe allergies
- Avoid in patients with blood disorders
- Elderly – increased risk of serious side effects
- G6PD deficiency (risk of haemolytic anaemia)
- Pts who can't maintain adequate fluid intake
- Pts with a predisposition to folate deficiency or hyperkalaemia

Special Monitoring Requirements
2 weekly FBC and U's and E's
Reduce dose if patients Creatinine Clearance is <30mL/min

Side effects
Commons/Very common: Diarrhoea, headache, hyperkalaemia, nausea, rash
Uncommon: Vomiting
Rare: Agranulocytosis, bone marrow depression, hypoglycaemia and several others – consult BNF for full list
Co-trimoxazole is associated with rare but serious side effects. Discontinue immediately if blood disorders (including leukopenia, thrombocytopenia, megaloblastic anaemia, eosinophilia) or rash (including Stevens- Johnson syndrome, toxic epidermal necrolysis, photosensitivity) develop.

Interactions: consult the BNF for full lists under Trimethoprim and Sulfamethoxazole
Zidovudine, Lamivudine, Dapsone, Ciclosporin, Rifampicin, Pyrimethamine, Warfarin (monitor INR carefully)
Phenytoin, Repaglinide, Digoxin or Amiodarone, Methotrexate, Azathioprine, Mercaptopurine
Caution should be exercised in patients taking any other drugs that can cause hyperkalaemia.e.g ACE inhibitors, Angiotensin 2 antagonists

Counselling Points
Take co-trimoxazole with food or drink. This will help prevent nausea and diarrhoea.
Although it's better to take with food you can take on an empty stomach.

Drink plenty of fluids when taking co-trimoxazole
Discontinue immediately if rash develops (including Stevens-Johnsons syndrome, toxic epidermal necrolysis, photosensitivity). This can develop initially as reddish target- like spots or circular patches often with central blisters on the trunk. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). The highest risk for occurrence of serious skin reactions is within the first weeks of treatment. If patient develops a rash or these skin symptoms, stop taking Co-Trimoxazole, seek urgent advice from a doctor and tell them that you are taking co-trimoxazole

1. Introduction

1.1. Rationale

Many patients with diabetes present with foot infections which require empirical antibiotic treatment to prevent serious complications. There are no trials that offer definitive advice on appropriate antibiotic treatment for the treatment of foot infections in people with diabetes. This guideline incorporates guidance given in the IDSA guidelines 'Diagnosis and Treatment of Diabetic Foot Infections' published in 2012 and the IWGDF guidelines published in 2023. See references below. Local resistance patterns have also been taken into account as has the risk/benefit ratio of prescribing antibiotics that may cause a high likelihood of *Clostridioides difficile* (*C.diff)* infection.

This guideline is for use as *empirical 1st line therapy* and the choice of antimicrobial agents may need to change when microbiological sensitivity data becomes available.

1.2. Objective

The objective is to offer antibiotic guidance on the empirical treatment of diabetes related foot infections.

1.3. Scope

This guideline covers the use of antimicrobial management for adult patients with diabetic foot infections at the NNUH. It excludes paediatrics

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
ACE	Angiotensin-converting enzyme
C-diff	Clostridioides difficile
CRP	C-Reactive protein
ESR	Erythrocyte sedimentation rate
FBC	Full blood count
IDSA	Infectious Disease Society of America
INR	International Normalised ratio
IWGDF	International Working group on the Diabetic Foot
IV	Intra-venous
LFTs	Liver Function Tests

MRSA	Methicillin Resistant *Staphylococcus aureus*
NNUH	Norfolk and Norwich University Hospitals NHS Foundation Trust
PO	Oral
STAT	Immediate one off dose
WBC	White blood cell

2. Responsibilities

2.1 Medical staff

Medical staff are responsible for prescribing antibiotic treatment according to this guideline

2.1. Nursing staff

Nursing staff are responsible for administering antibiotic treatment according to this guideline

2.2. Pharmacists

Pharmacists are responsible for checking prescriptions and administration against this guideline

3. References

Lipsky B, Berendt A et al, 2012. Infectious Diseases Society of America Clinical Practice Guideline for the diagnosis and treatment of diabetic foot infections CID. 54;12:e132-e173.
SIGN Guideline 116 (Sept 2013) http://www.sign.ac.uk/pdf/sign116.pdf

NICE Guidance NG19 (Aug 2015): Diabetic foot problems: prevention and management. http://www.nice.org.uk/guidance/ng19

Gooday C, Hallam C, Sieber C *et al.* An antibiotic formulary for a tertiary care foot clinic: admission avoidance using intramuscular antibiotics for borderline foot infections in people with diabetes. *Diabetic Med* 2013; **30**(5)**:**581-589

Lipsky B, Silverman M, Joseph W. A Proposed New Classification of Skin and Soft Tissue Infections Modeled on the Subset of Diabetic Foot Infections. Open Forum Infectious Diseases. 1-8

https://iwgdfguidelines.org/wp-content/uploads/2023/07/IWGDF-2023-04-Infection-Guideline.pdf

4. Audit of the process

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
Prescribing according to policy	Audit	Diabetic foot team	Diabetic Foot dept	Yearly
Datix reports	Ad hoc	Antimicrobial Pharmacist	Diabetic Foot dept	Ongoing

The audit results are to be discussed at relevant governance meetings to review the results and recommendations for further action. Then sent to the Antimicrobial Subcommittee who will ensure that the actions and recommendations are suitable and sufficient.

5. Appendices

There are no appendices for this document.

6. Equality Impact Assessment (EIA)

Type of function or policy	Existing

Division		**Department**	
Name of person completing form	Caroline Hallam	**Date**	9/11/23

Equality Area	Potential Negative Impact	Impact Positive Impact	Which groups are affected	Full Impact Assessment Required YES/NO
Race				No
Pregnancy & Maternity	Certain antibiotics contra-indicated or to be used with caution in pregnancy	Certain antibiotics contra-indicated or to be used with caution in pregnancy	Certain antibiotics contra-indicated or to be used with caution in pregnancy	
Disability				
Religion and beliefs				
Sex				
Gender reassignment				
Sexual Orientation				
Age				
Marriage & Civil Partnership				
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.