

Guidelines for the management of Diabetic Foot Infection

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Summary of Recommendations

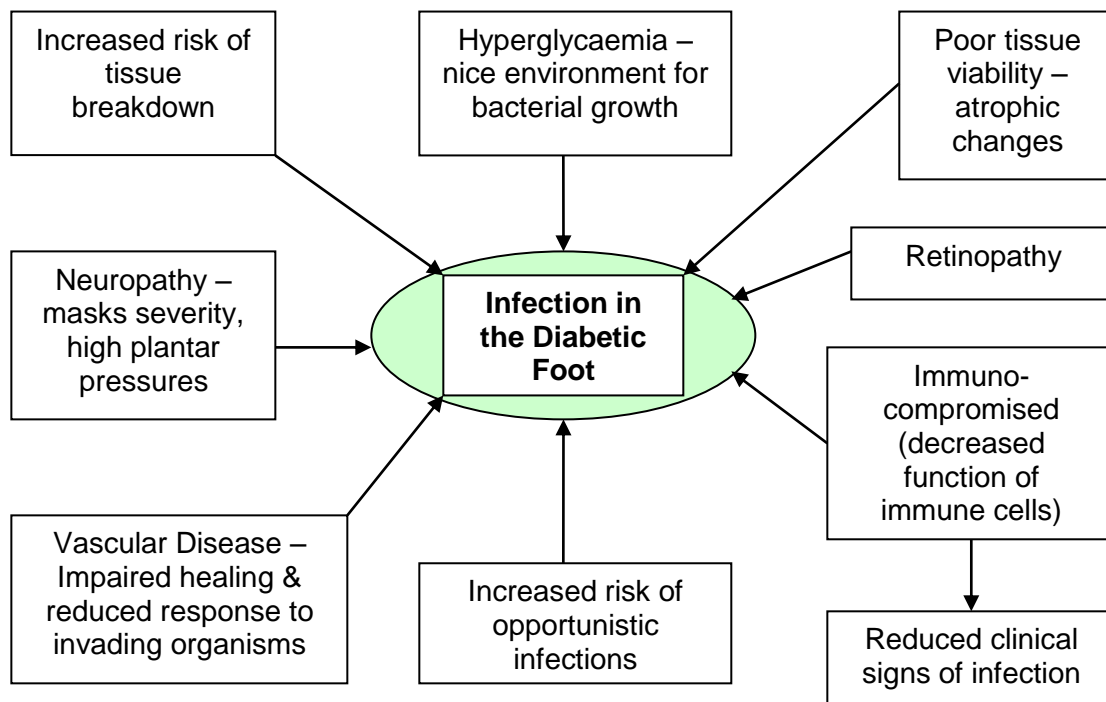
- All patients presenting with diabetic foot infection should be referred to a member of the multidisciplinary team for expert assessment within 24 hours.
- Where clinical infection is suspected microbiological sampling is advocated particularly in those with chronic infections or who have recently been treated with antibiotics.
- Diagnosis of an infection should be based on clinical findings. Cultures are meant to identify organisms and to assist in treatment of an infection rather than be used to diagnose infection.
- When clinical signs of infection are present the patient should be issued immediately with an empiric antibiotic regimen on the basis of the severity of the infection and the likely pathogen/s.
- Non-infected diabetic foot ulceration do not require antibiotics, however appropriate wound care and management by a member of the multidisciplinary foot care team should be instigated.
- Where oral antibiotic issue is advocated this should initially be for 2 weeks, with a clinical review set within 1 week to assess clinical response and assess any microbiological findings.
- Antibiotic therapy should continue until, but not beyond, resolution of clinical findings of infection.
- If antibiotic courses are prolonged over 2 weeks duration renal and liver function should be monitored regularly and adjustments made accordingly.

Introduction

People with diabetes are at high risk of infection due to multiple factors (see figure 1). Impaired leukocyte chemotaxis and phagocytosis is compounded by high glucose levels and poor tissue perfusion. The decreased ability to fight off infection combined with tissue hypoxia is thought to create an ideal environment for a necrotizing infection (Murray and Boulton, 1995; Gilchrist, 1997).

Foot infections in diabetes patients rank among the most common infectious complications that require hospitalisation and are a frequent cause of lower extremity amputation (Boulton, 2005). For example in a 2 year study by Lavery and co-workers for the 151 patients who developed diabetic foot infection there was a 56 fold increase in risk of hospitalisation and 155 fold increase in risk of amputation (Lavery et al 2006).

Figure 1- Combined effects leading to the increased risk of infection in the diabetic foot



Diagnosing Infection in the Diabetic Foot

The international working group on the diabetic foot and the infectious disease society of America (IDSA) have outlined clinical criteria for diagnosing diabetic foot infections and classifying severity (see figure 2). This classification system has been validated (Lavery et al, 2007) and found to have a significant correlation between the defined severity of the infection and risk of amputation, anatomical level of amputation and hospitalisation. However, it is recognised that clinical signs and symptoms of infection in the diabetic patient may be subdued due to pre-existing peripheral arterial disease, peripheral neuropathy and impaired host response to infection, making diagnosis complicated. In this situation, some evidence supports the correlation of additional or secondary findings, for example, non-purulent secretions, friable or discoloured granulation tissue, undermining of the wound edges, or a foul odour, with evidence of infection (Gardner, 2009). As recommended by NICE guidance NG19 (2015) specialist assessment of diabetic foot ulceration and infection should always be sought by the multidisciplinary diabetic foot team within 24 hours of presentation. Locally to arrange an urgent follow-up for a diabetes patient we have an on call phone line (07948 429804) and email access via referral.bookingservice@nhs.net

It has been repeatedly reported that patients with deep foot infections which are potentially limb threatening often do not have fever, leukocytosis increase in the white blood cell count or markedly elevated acute phase serum markers and so the absence of these findings does not necessarily exclude a potentially serious infection. Worsened glycemic control is often the only systemic evidence of a serious infection in this setting (Armstrong et al, 1996; Eneroth et al, 1999).

Figure 2 – Classification of Diabetic foot Infection (IDSA)

Classification	Definition
Grade 1 (Uninfected)	No symptoms or signs of infection
Grade 2 (Mild)	Infection involving the skin and subcutaneous tissue only, with no involvement of deeper tissues and no systemic signs and symptoms. Exclude other causes of an inflammatory response (e.g. gout, trauma, acute Charcot neuro- osteoarthropathy, fracture, thrombosis, venostasis). At least two of the following manifestations are present: <ul style="list-style-type: none"> • Localised swelling or induration • Erythema >0.5–2 cm around the ulcer • Local tenderness or pain • Local warmth • Purulent discharge
Grade 3 (Moderate)	<ul style="list-style-type: none"> • Infection involving structures deeper than skin and subcutaneous tissues (e.g. abscess, osteomyelitis, septic arthritis, or necrotizing fasciitis) • Erythema (cellulitis) extending >2 cm around an ulcer in addition to one of the following: oedema, tenderness, heat, purulent discharge • No signs of a systemic inflammatory response as shown in the grade 4 infection
Grade 4 (Severe)	Any foot infection with signs of a systemic inflammatory response syndrome (SIRS), manifested by two or more of the following: <ul style="list-style-type: none"> • Temperature <36 °C or >38 °C • Heart rate >90 beats/min • Respiratory rate >20 beats/min or PaCO₂ <32 mmHg • White blood cell count <4000 or >12 000 cells/μL or ≥10% immature (band) forms

(Lipsky et al 2012)

Microbiology of the Diabetic Foot

Isolation of antibiotic-resistant organisms, particularly MRSA but also extended-spectrum β -lactamase (ESBL)–producing gram-negative bacilli and highly resistant *Pseudomonas aeruginosa*, is an increasing problem with diabetic foot infection (Dang et al, 2003; Edmonds, 2005, Richard et al, 2008). Antibiotics used indiscriminately and without need results in an increased probability of developing resistance (Jenseni et al, 1995) and hence the use of antibiotics without the clinical suspicion of the presence of infection is not appropriate. However, the high morbidity and mortality associated with infected diabetic ulcers suggest that when clinical signs of infection are suspected then the patient should be issued immediately an empiric antibiotic regimen on the basis of the severity of the infection and the likely causative pathogens.

In patients with a clinically infected wound, properly obtained wound cultures provide highly useful information for guiding antibiotic therapy, particularly in those with chronic infections or who have recently been treated with antibiotics (Nelson et al, 2006). Tissue samples obtained by biopsy or curettage after the wound has been cleansed and debrided is the most accurate and therefore advocated method of microbiological sampling (Lipsky et al, 2012). Although obtaining swab specimens is more convenient and require less training/skill, they provide less accurate results, particularly if the wound has not been properly debrided. However, if swabbing is the method available at the time of presentation then the accuracy of the results will depend on how the sample is obtained and the general principles in figure 3 should be followed (Gardner et al, 2006).

The majority of mild infections that have not previously been treated are caused by aerobic gram positive cocci, with *Staphylococcus aureus* being the most common isolate. Therefore it is important for empiric treatment to have good aerobic gram positive cover (Lipsky et al, 1990). However, mild infections that have been previously treated are more likely to be complicated by the addition of gram negative bacteria and hence often warrant a broader spectrum of cover initially. It is noted in the literature that obligate anaerobic organisms are isolated from many chronic, previously treated, or severe infections (Wheat et al, 1986; Ng et al 2008), but they are not usually major pathogens in most mild to moderate infections (Armstrong et al, 1995). Treatment with oral antibiotic agents (preferably ones with high bioavailability) is often appropriate for mild to moderate infections in patients without gastrointestinal absorption problems and for whom an oral agent with the appropriate spectrum is available (Lipsky et al, 2012).

Moderate and severe infections, particularly those that have been previously treated or complicated by the presence of peripheral arterial disease are likely to be polymicrobial in nature and hence it is considered safest to promptly commence therapy with a broad-spectrum regimen of adequate strength and bioavailability to penetrate deep structures at the periphery (Lipsky et al, 2012). The antibiotic agent(s) should have activity against gram-positive cocci, as well as common gram-negative and obligate anaerobic organisms. To ensure adequate tissue concentrations for extensive moderate infections and severe infections it is advocated that it is safest to start with parenteral therapy, which can usually be switched to oral treatment within a few days when the patient is systemically well and culture results are available to guide the selection.

Figure 3 - Swab Technique

Diagnosis of an infection should be based on clinical findings. Cultures are meant to identify organisms and to assist in treatment of an infection rather than be used to diagnose infection as only wound surface organisms are sampled (as opposed to organisms within the tissue) (Tammellin et al, 1998). No particular method of wound swabbing can be considered definitive, however the literature recommends the following principles:

Principle	Rationale
DO NOT use antiseptic solutions prior to taking wound swab (Kiernan 1998; Cuzzell 1993).	Organisms will be killed, and a false negative result may occur (Cuzzell 1993).
DO NOT use local anaesthetic prior to taking a swab.	Local anaesthetics can demonstrate antibacterial effects (Gilchrist 1996).
DO NOT culture pooled exudate or wound dressings (Cuzzell 1993)	Risk of non-wound contaminants is high.
DO remove excessive debris and all dressing residue without unduly disturbing the wound surface using a gentle stream of normal saline (Lawrence 1998; Donovan 1998; Cooper and Lawrence 1996).	Surface organisms are often different to those causing the wound infection and skin cells and other harmless contaminants may be present on the wound surface (Cuzzell1993).
DO wait for 1-2 minutes before taking swab (Lawrence 1999). If wound is fairly dry, moisten swab with sterile normal saline, if wound is moist the swab can be used dry.	Allows organisms to rise to the surface of the wound. Maximisation of uptake of exudate by swab.
DO take wound swabs from an area of viable tissue where the clinical signs of infection are present i.e. do not swab eschar or yellow, fibrous slough (Kiernan 1998; Cuzzell1993).	Infection causing organisms are most likely to be found in viable tissue.
DO use a zig-zag motion to swab wound surface and rotate swab during swabbing (Donovan1998; Lawrence 1999). Whole wound surface should be swabbed. If wound is very large, swabbing a number of small areas is acceptable (Gilchrist 2000).	Will allow for most complete sampling of wound organisms.
DO avoid surrounding skin (Kiernan1998; Cuzzell 1993).	Will avoid introducing superficial skin organisms into the culture.
DO transport swab to pathology laboratory as quickly as possible. If a delay of more than 24 hours is expected between taking a wound swab and arrival at the laboratory it is advised to store the swab in a refrigerator at 4°C (Cooper and Lawrence 1996)	Assists in preservation of common wound bacteria.

Antibiotic Selection

There is an absence of well controlled clinical trials for antibiotics in diabetic foot infection. This is largely thought to be because study design is particularly challenging. There is great patient to patient variability in terms of vascular supply, existing co-morbidities, extent and duration of infection and there are a lack of standardised definitions for infections, improvement and cure, especially when surgical intervention is included in the protocol (Jeffcoate et al, 2008), These factors make it difficult to provide clear-cut recommendations regarding antibiotic therapy in the case of diabetic foot infection and hence there are no national guidance specific to this condition on which to rely. This is compounded by the fact that critical reviews of published clinical trials of antibiotic regimens for diabetic foot infections have concluded that there are no standardised treatment recommendations and optimal therapy should rely on local knowledge of the likely pathogens and the spectrum of antibiotics that can provide coverage (Roberts and Simon 2012; Crouzet et al 2011 and Lipsky et al 2004).

Following IDSA guidelines antibiotic therapy should continue until, but not beyond, resolution of clinical findings of infection. It is suggested that an initial oral antibiotic course for mild to moderate infection of 2 weeks is appropriate and seeking urgent admission for IV antibiotic therapy and assessment of the need for surgical drainage and debridement in those presenting with severe infections (Lipsky et al, 2012).

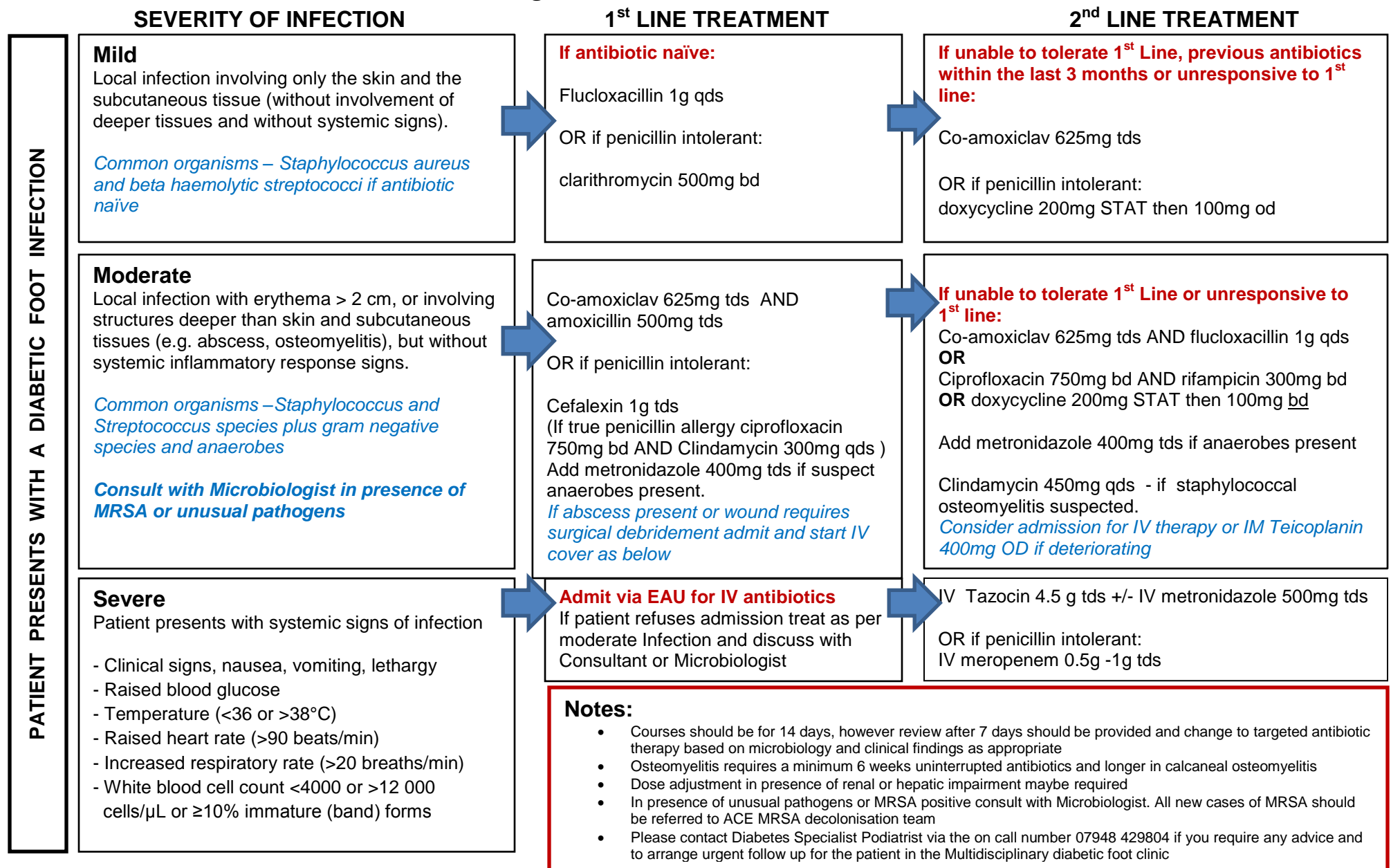
Due to these issues local agreement has been sought to provide clear guidance for staff with regards to first and second line antibiotic choices when presented with Diabetic Foot Infection (Figure 4).

MRSA

If swab result is returned MRSA positive immediately change antibiotics to doxycycline 200mg stat followed by 100mg bd (presuming reported as tetracycline sensitive). Consult with microbiologist if renal or liver impairment present or tetracycline resistant.

All new cases of MRSA, should be referred to the ACE MRSA decolonisation team.

Figure 4 – Antibiotic Guidance



Special Considerations

Antibiotic	Comments	Precautions	
		Hepatic Impairment	Renal Impairment
Amoxicillin	Risk of <i>Clostridium difficile</i> *. Amoxicillin can reduce the excretion of methotrexate (increased risk of toxicity). Amoxicillin potentially alters the anticoagulant effect of warfarin & phenindione – monitor INR and adjust dose accordingly.	Rarely causes cholestatic jaundice	If GFR 10-30ml/min/1.73m ² reduce to 500mg bd If GFR less than 10ml/min maximum 500mg daily
Cefalexin	Avoid if history of serious hypersensitivity reaction to penicillins. Risk of <i>Clostridium difficile</i> *.	Nil	If eGFR 40-50ml/min/1.73m ² max 1g tds If eGFR 10-40ml/min/1.73m ² max 500mg tds If eGFR less than 10ml/min/1.73m ² max 250mg tds
Ciprofloxacin	Risk of <i>Clostridium difficile</i> *. Do NOT use in pregnant or breastfeeding women. Use with caution in patients with epilepsy, myasthenia gravis G6PD deficiency. Milk, indigestion remedies, iron and zinc should not be taken 2 hours before and after taking ciprofloxacin. Multiple significant interactions – refer to BNF appendix 1.	Nil	If eGFR 30-60ml/min/1.73m ² reduce dose to: 500mg bd If eGFR under 30ml/min/1.73m ² 500mg od
Clarithromycin	Avoid use in pregnant or breastfeeding women. Do not prescribe modified release formulations. Multiple significant interactions – refer to BNF appendix 1.	Avoid in severe impairment if renal impairment also present	If eGFR under 30ml/min/1.73m ² , reduce dose to 250mg bd. Maximum duration 14 days. Avoid if severe hepatic impairment also present.
Clindamycin	Risk of <i>Clostridium difficile</i> *. Monitor liver and renal function where treatment exceeds 10 days.	Nil	Nil

* Risk of *Clostridium difficile* in the elderly and previously hospitalised due to its broad spectrum of activity, discontinue immediately in the presence of bloody or severe diarrhoea, start metronidazole and seek microbiological advice.

Antibiotic	Comments	Precautions	
		Hepatic Impairment	Renal Impairment
Co-amoxiclav	Risk of <i>Clostridium difficile</i> *. Co-amoxiclav can reduce the excretion of methotrexate (increased risk of toxicity). Co-amoxiclav can reduce the excretion of methotrexate (increased risk of toxicity). Co-amoxiclav potentially alters the anticoagulant effect of warfarin & phenindione – monitor INR and adjust dose accordingly.	Cholestatic jaundice can occur. Use with caution and monitor liver function if treatment should exceed 14 days.	Reduction of dose if eGFR 10-30ml/min/1.73m ² to 625mg bd If eGFR <10ml/min/1.73m ² 625mg od
Doxycycline	Should NOT be given to pregnant or breast feeding women. Indigestion remedies, iron and zinc reduce the absorption – patients should be advised to leave a 2 hour gap before/after taking doxycycline. Patients should be advised to protect skin from sunlight. The effects of coumarins and phenindione may be enhanced by doxycycline (monitor INR). Avoid concomitant use with retinoids.	Avoid or use with caution	Use with caution (avoid excessive doses)
Flucloxacillin	High rates of gastric disturbance at high doses consider change of antibiotic if patient unable to tolerate adequate dose. Should be taken on an empty stomach at least 1 hour before food or 2 hours after food. Flucloxacillin can reduce the excretion of methotrexate (increased risk of toxicity). Flucloxacillin potentially alters the anticoagulant effect of warfarin & phenindione – monitor INR and adjust dose accordingly	Use with caution. Monitor liver function during prolonged courses.	Reduction of dose if eGFR under 10ml/min/1.73m ² . Monitor renal function during prolonged courses.
Metronidazole	Avoid high doses in pregnant or breastfeeding women. Disulfiram-like reaction with alcohol. Take with or after food. The effects of coumarins may be enhanced by metronidazole. There is a risk of toxicity with some cytotoxics – see BNF appendix 1.	In severe liver impairment reduce dose to one-third (1/3) and give once daily	Nil
Rifampicin	Risk of liver disorder, patients should be told how to recognize signs of liver disorder (persistent nausea, vomiting, malaise or jaundice), if symptoms occur discontinue treatment immediately. Should be taken 1 hour before food or 2 hours after. A reddish coloration of the urine, sweat, sputum and tears occurs and the patient should be forewarned of this. Soft contact lenses have been permanently stained. Multiple significant interactions – refer to BNF appendix 1.	Avoid or do not exceed 8 mg/kg daily. Monitor liver function.	Use with caution if daily dose over 600mg. Consider a dose reduction if eGFR under 10ml/min/1.73m ²

* Risk of *Clostridium difficile* in the elderly and previously hospitalised due to its broad spectrum of activity, discontinue immediately in the presence of bloody or severe diarrhoea, start metronidazole and seek microbiological advice.

Reference: BNF online, Electronic Medicines Compendium, Renal Drug Handbook 3rd edition.

Referral Information

Referral to Community Podiatry or MDT foot clinic through NEEDS referral form (see appendix A)

Telephone – 0345 2413313 or 01473 344930 (option 2)

Email - referral.bookingservice@nhs.net

Community Podiatry - Monday to Friday, operates from 11 locations across North East Essex

Step up/step down clinic to MDT foot – Thursday afternoon, NEEDS, 1st floor Bluebell surgery, Highwoods, Colchester

Multidisciplinary Diabetic foot clinic – Monday and Friday mornings, Colchester General Hospital Outpatients Department

Podiatry on call number for urgent Diabetic foot problems - 07948 429804

Appendix A - Application for Podiatry or MDT Foot Clinic Assessment

NEEDS Referral Form

NHS Number: Referral Date:

Patient Consent : Yes No Year of Care Plan Agreed : Yes No
 Does the patient require an interpreter Yes No **Do they have any specific sharing preferences?.** Yes No
 Housebound Yes No For example contact carer directly or do not call home etc

Patient Name: Address:
 Tel: Mobile: Postcode:
 DOB: Gender: M F Ethnicity:

Registered: GP Practice Details: **Clinical Referrers Details Name and designation**
Type of Diabetes: Type 1: Type 2: Other: **Notification of newly diagnosed T2 ONLY:** Yes No
 Date of diagnosis ___ / ___ / ___

Referral Reason and comments (please give as much information as possible and tick one box below)
Please attach list of current medication, medical history and any blood glucose readings

History of Mental Illness

Type 1 education: DAFNE <input type="checkbox"/> 3-hour carbohydrate counting (only for those unable to complete DAFNE or previously attended DAFNE) <input type="checkbox"/>	Type 2 education: On insulin? Yes <input type="checkbox"/> No <input type="checkbox"/>
Diabetes Dietary advice / carbohydrate counting <input type="checkbox"/>	Recurrent Hypoglycaemia <input type="checkbox"/>
Community Diabetes Podiatry (please also complete part b *Moderate/High Risk) <input type="checkbox"/>	MDT Urgent Foot MDT (please also complete part b *Emergency Foot) <input type="checkbox"/>
Diabetes in Pregnancy How many weeks gestation or due date <input type="checkbox"/>	Diabetes - Planning Pregnancy <input type="checkbox"/>
Abnormal GTT in Pregnancy <input type="checkbox"/>	Fasting GTT 2 Hour GTT Date

Care Process	Result	Date	Care Process	Result	Date
Smoking Status			Blood Pressure		
Height			Weight		
Foot Risk Assessment: Part B <u>Must be completed</u>			Have all 8 care processes been completed: Yes <input type="checkbox"/> No <input type="checkbox"/>		

Send to referral.bookingservice@nhs.net

Part B * Diabetic Foot Referrals

Name:.....	NHS No:	DoB:
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Please indicate the patient's NICE (2016) foot risk category in the box below
*** If not completed, referral will be rejected**

Low Risk	Moderate Risk	High Risk	Active Foot Disease
<input type="checkbox"/> <ul style="list-style-type: none"> ▪ Normal Sensation and no evidence of peripheral neuropathy AND ▪ Palpable Pulses and no signs of ischaemia AND ▪ No evidence of foot deformity ▪ If nail cutting required patient to seek through HCPC registered private podiatry or Age UK service ▪ ONLY refer to Podiatry for a specific Podiatric need e.g. biomechanics 	<input type="checkbox"/> <ul style="list-style-type: none"> ▪ Neuropathy OR ▪ Non-critical limb ischaemia OR ▪ Foot Deformity ▪ (Deformity often accompanied by tissue changes e.g. red area or pathological callus or corns) 	<input type="checkbox"/> <ul style="list-style-type: none"> ▪ Previous foot ulcer or amputation OR ▪ On renal replacement therapy OR ▪ Combination of Foot deformity /callus with Neuropathy OR ▪ Combination of foot deformity / callus with non-critical limb Ischaemia OR ▪ Combination of Non-Critical Limb ischaemia & Neuropathy 	<input type="checkbox"/> <ul style="list-style-type: none"> ▪ Foot ulceration OR ▪ Suspicion of an acute Charcot arthropathy OR an unexplained hot, red, swollen foot with or without pain If presenting with any of the below consider admission via EAU, phone on call number if need advice 07948 429804 ▪ Spreading infection / with or without systemic symptoms OR ▪ Critical limb ischaemia OR Gangrene

Inform patient of their risk category and provide verbal advice / foot risk leaflet

Foot Pathology / Reason for referral (please give as much information as possible) any concerns
telephone on-call Number 07948 429804

Send to referral.bookingservice@nhs.net

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