Empiric Antimicrobial Therapy for Diabetic Foot Infection
(NB Provincial Health Authorities Anti-Infective Stewardship Committee, September 2019)

Infection Severity	Preferred Empiric Regimens	Alternative Regimens	Comments
Mild • Cellulitis **less than 2 cm** and without involvement of deeper tissues • Non-limb threatening • No signs of sepsis	Wound **less than 4 weeks** duration:[d] • cephalexin 500 – 1000 mg PO q6h*[,a] **OR** • cefadroxil 500 – 1000 mg PO q12h*[,a] True immediate allergy to a beta-lactam at risk of cross reactivity with cephalexin or cefadroxil: • cefuroxime 500 mg PO q8–12h*[,b]	Wound **less than 4 weeks** duration:[e] • clindamycin 300 – 450 mg PO q6h (only if severe delayed reaction to a beta-lactam) MRSA Suspected: • doxycycline 200 mg PO for 1 dose then 100 mg PO q12h **OR** • sulfamethoxazole+trimethoprim 800+160 mg to 1600+320 mg PO q12h*[,f]	• Outpatient management recommended • Tailor regimen based on culture and susceptibility results and patient response
	Wound **greater than 4 weeks** duration:[d] • amoxicillin+clavulanate 875/125 mg PO q12h*[,c] **OR** • cefuroxime 500 mg PO q8–12h*[,b] AND metroNIDAZOLE 500 mg PO q12h	Wound **greater than 4 weeks** duration[e] and MRSA suspected: • doxycycline 200 mg PO for 1 dose then 100 mg PO q12h AND metroNIDAZOLE 500 mg PO q12h **OR** • sulfamethoxazole+trimethoprim 800+160 mg to 1600/320 mg PO q12h*[,f] AND metroNIDAZOLE 500 mg PO q12h	
Moderate • Cellulitis **greater than 2 cm** or involvement of deeper tissues • Non-limb threatening • No signs of sepsis	Wound **less than 4 weeks** duration:[d] • ceFAZolin 2 g IV q8h*[,b] **OR** • cefTRIAXone 2 g IV q24h[b] (to facilitate outpatient management when ambulatory administration of ceFAZolin not possible)	Wound **less than 4 weeks** duration:[e] • levoFLOXacin 750 mg IV/PO q24h* MRSA suspected: • vancomycin 25 to 30 mg/kg IV x 1 dose, then 15 mg/kg IV q8–12h (adjust dose to a target trough of 10 to 15 mg/L)*	• Initial management with outpatient parenteral therapy with rapid step-down to oral therapy after 48 to 72 hours based on patient response recommended • Tailor regimen based on culture and susceptibility results and patient response
	Wound **greater than 4 weeks** duration:[d] • ceFAZolin 2 g IV q8h*[,b] AND metroNIDAZOLE 500 mg PO q12h **OR** • cefTRIAXone 2 g IV q24h[b] AND metroNIDAZOLE 500 mg PO q12h	Wound **greater than 4 weeks** duration:[e] • levoFLOXacin 750 mg IV/PO q24h* AND metroNIDAZOLE 500 mg PO q12h MRSA suspected, add: • vancomycin 25 to 30 mg/kg IV x 1 dose, then 15 mg/kg IV q8–12h (adjust dose to a target trough of 10 to 15 mg/L)*	
Severe • Signs of sepsis • Limb or foot threatening • Extensive soft tissue involvement or deeper tissues (i.e. bone, joint or tendon spaces) • Pulseless foot	• piperacillin+tazobactam 4.5 g IV q6h*[,c] MRSA suspected, add: • vancomycin 25 to 30 mg/kg IV x 1 dose, then 15 mg/kg IV q8–12h (adjust dose to a target trough of 10 to 15 mg/L)*	• meropenem 500 mg IV q6h*[,b] **OR** • levoFLOXacin 750 mg IV q24h* AND metroNIDAZOLE 500 mg IV/PO q12h MRSA suspected, add: • vancomycin 25 to 30 mg/kg IV x 1 dose, then 15 mg/kg IV q8–12h (adjust dose to a target trough of 10 to 15 mg/L)*	• Inpatient management recommended • Urgent vascular assessment if pulseless foot • Tailor regimen based on culture and susceptibility results and patient response

Duration and Route of Therapy – dependent on site, severity and extent of infection as well as other patient specific factors such as degree of surgical management and vascular status.

Site of Infection, by Severity or Extent	Route of Administration	Duration of Therapy	Comments
Soft Tissue Only			
Mild	Oral	1 – 2 weeks	
Moderate	Initial parenteral with rapid oral step down within 48 to 72 hours	1 – 2 weeks	• May extend if slow to resolve
Severe	Initial parenteral, switch to oral when or if possible	2 – 4 weeks	• Longer duration and IV route recommended for extensive infections involving deeper tissues (i.e. tendon spaces)
Bone or Joint Involvement			
No residual infected tissue (e.g. post-amputation)	Parenteral or Oral	2 – 5 days post-amputation	
Residual infected soft tissue (but no bone)	Parenteral or Oral	1 – 4 weeks	• Longer duration and IV route recommended if severe and infections involving deeper tissues (i.e. tendon spaces)
Residual infected but viable bone (incomplete surgical resection)	Parenteral (oral switch only if high bioavailability and good bone penetration)	4 – 6 weeks	
No surgical debridement or residual dead bone postoperatively	Initial parenteral therapy, then consider oral switch	Greater than or equal to 3 months (i.e. 6 weeks IV, followed by 6 weeks PO)	

Clinical Pearls

- Debridement, good glycemic control, proper wound care, vascular assessment and smoking cessation are essential for the management of diabetic foot infections
- In a clinically infected wound a positive probe-to-bone (PTB) test is highly suggestive of osteomyelitis.
- Imaging: recommend to start with plain radiography (radionuclide imaging generally not necessary)
- Cultures: prefer tissue specimens post-debridement and cleansing of wound; surface or wound drainage swabs not recommended
- Consider prior wound microbiology results when selecting an empiric therapy
- MRSA risk factors: history of MRSA infection or colonization, household contact with a MRSA colonized individual, IV drug use, homelessness, incarcerated persons, recent travel to or residing in an MRSA endemic region or community

[a] Avoid if true immediate Type-1 (IgE-mediated) hypersensitivity reaction to a beta-lactam at risk of cross reactivity with cephalexin or cefadroxil (i.e. allergy to ampicillin, amoxicillin, cefaclor or cefprozil)

[b] Appropriate therapy option for patients with an immediate Type-1 (IgE-mediated) hypersensitivity reaction to penicillin (i.e. anaphylaxis, angioedema, laryngeal edema, urticaria)

[c] Avoid in patients with immediate Type-1 (IgE-mediated) hypersensitivity reaction to penicillin, significant risk of cross-reactivity exists.

[d] Usual core pathogens for infections that have an acute onset (i.e. less than 4 weeks) include: Gram-positive organisms such as beta-hemolytic *Streptococci* and *Staphylococcus aureus*

[e] Usual core pathogens for chronic or more complex infections (i.e. greater than 4 weeks) include: Gram-positive and Gram-negative organisms as well as anaerobes

[f] Use caution and consider avoiding in patients with pre-existing renal disease, elderly patients or those receiving an angiotensin-converting-enzyme inhibitor, angiotensin receptor blocker, amiloride or spironolactone due to the risk of hyperkalemia

*Dose adjustment required in renal impairment

References:

1. Bowering K, Embil JM. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Foot Care. Can J Diabetes 37(2013) S145-S149
2. Lipsky BA, Berendt AR, Cornia PB et al. 2012 Infectious Disease Society of America Clinical Practice Guidelines for the Diagnosis and Treatment of Diabetic Foot Infections. CID 2012:54(12):132-173
3. Lipsky BA, Armstrong DG, Citron DM et al. Ertapenem versus piperacillin/tazobactam for diabetic foot infections (SIDESTEP): prospective, randomized, controlled, double-blinded, multicentre trial. Lancet 2005; 366:1695 – 1703
4. Blond-Hill E, Fryters S. Bugs & Drugs An Antimicrobial/Infectious Diseases Reference. 2012. Alberta Health Services