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

<table>
<thead>
<tr>
<th>Infection Severity</th>
<th>Preferred Empiric Regimens</th>
<th>Alternative Regimens</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **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:**  
• cephalaxin 500 – 1000 mg PO q6h*  
• cefadroxil 500 – 1000 mg PO q12h*  
True immediate allergy to a beta-lactam at risk of cross reactivity with cephalaxin or cefadroxil:  
• cefuroxime 500 mg PO q8–12h* | **Wound less than 4 weeks duration:**  
• 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* |
| | **Wound greater than 4 weeks duration:**  
• amoxicillin+clavulanate 875/125 mg PO q12h* OR  
• cefuroxime 500 mg PO q8–12h* AND metronIDAZOLE 500 mg PO q12h | | |
| | **Wound greater than 4 weeks duration** 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* 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:**  
• ceFAZolin 2 g IV q6h* OR  
• ceFTRIAXone 2 g IV q24h* (to facilitate outpatient management when ambulatory administration of ceFAZolin not possible) | **Wound less than 4 weeks duration:**  
• levoFLOXacin 750 mg IV/PO q24h* |
| | **Wound greater than 4 weeks duration:**  
• ceFAZolin 2 g IV q6h* AND metronIDAZOLE 500 mg PO q12h OR  
• ceFTRIAXone 2 g IV q24h* AND metronIDAZOLE 500 mg PO q12h | | Initial management with outpatient parenteral therapy with rapid step-down to oral therapy after 48 to 72 hours based on patient response recommended |
| | **Wound greater than 4 weeks duration** and MRSA suspected:  
• vancomycin 25 to 30 mg/kg IV x 1 dose then 15 mg/kg IV q8–12h (adjust dose to a trough target of 15 to 20 mg/L)* |
| | **Wound greater than 4 weeks duration** and MRSA suspected, add:  
• vancomycin 25 to 30 mg/kg IV x 1 dose then 15 mg/kg IV q8–12h (adjust dose to a trough target of 15 to 20 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  
MRSA suspected, add:  
• vancomycin 25 to 30 mg/kg IV x 1 dose then 15 mg/kg IV q8–12h (adjust dose to a trough target of 15 to 20 mg/L)* | **Wound less than 4 weeks duration:**  
• meropenem 500 mg IV q6h* OR  
• levoFLOXacin 750 mg IV q24h* AND metronIDAZOLE 500 mg IV/PO q12h |
| | | **Wound greater than 4 weeks duration** and MRSA suspected:  
• meropenem 500 mg IV q6h* AND levoFLOXacin 750 mg IV q24h* AND metronIDAZOLE 500 mg IV/PO q12h |
| | | | Inpatient management recommended  
Urgent vascular assessment if pulseless foot  
Tailor regimen based on culture and susceptibility results and patient response |

* Any adverse effects:** PO** = Oral, **IV** = Intravenous
**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.

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

**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.
- 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).
- Appropriate therapy option for patients with an immediate Type-1 (IgE-mediated) hypersensitivity reaction to penicillin (i.e. anaphylaxis, angioedema, laryngeal edema, urticaria).
- Avoid in patients with immediate Type-1 (IgE-mediated) hypersensitivity reaction to penicillin, significant risk of cross-reactivity exists.
- 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*.
- 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.
- 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: