## GUIDELINES FOR TREATMENT OF NATIVE VALVE INFECTIVE ENDOCARDITIS IN ADULTS

(Infectious Diseases consultation is STRONGLY recommended)

<table>
<thead>
<tr>
<th>Empiric Therapy</th>
<th>Pathogens</th>
<th>Subsequent Therapy (Renal Dose Adjustments May Be Necessary)</th>
<th>Duration of Therapy</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Vancomycin IV4 + Ceftriaxone 2 g IV q24h | **Viridans group streptococci OR Streptococcus gallolyticus (bovis)** | Penicillin MIC ≤0.12 mg/L | Preferred:
Penicillin G 3 million units IV q4h | 4 weeks | • Avoid the 2-week regimen with gentamicin in patients with known cardiac or extracardiac abscess, CrCl <20 mL/min, impaired 8th cranial nerve function, or Abiotrophia, Granulicatella, or Gemella spp. Infection.  
• Gentamicin is used for gram positive synergy. For Viridans group streptococci and Streptococcus gallolyticus with penicillin MIC <0.5 mg/L, once daily gentamicin (3 mg/kg IV q24h) is preferred, with gentamicin trough goal ~1 mg/L.  
• In patients with renal insufficiency, dosing adjustments should be made with PharmD. |
| | Penicillin MIC >0.12-<0.5 mg/L | Preferred (if susceptible):
Ceftriaxone 2 g IV q24h | 4 weeks | • Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L.  
• In patients with renal insufficiency, dosing adjustments should be made with PharmD.  
• 4-week duration indicated only if symptoms of infection <3 month duration. |
| | Penicillin MIC ≥0.5 mg/L | Preferred (if susceptible):
Ceftriaxone 2 g IV q24h + Gentamicin IV³ | 4-6 weeks | • Request susceptibility testing for penicillin if used for therapy.  
• Ampicillin-aminoglycoside regimen: 4-week duration indicated only if symptoms of infection <3 month duration. |
| | Enterococci strains susceptible to penicillin and gentamicin | | | • Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L.  
• In patients with renal insufficiency, dosing adjustments should be made with PharmD.  
• 4-week duration indicated only if symptoms of infection <3 month duration. |
| | Enterococci strains resistant to penicillin and resistant to gentamicin | | | • Streptomycin dose 7.5 mg/kg IV q12h is preferred, with peak goal 20-35 mg/L and trough goal <5 mg/L.  
• In patients with renal insufficiency, dosing adjustments should be made with PharmD. |
| | Enterococci strains resistant to vancomycin, aminoglycosides, and penicillin | | | • Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred, with gentamicin peak goal 3-5 mg/L and trough goal <1 mg/L.  
• In patients with renal insufficiency, dosing adjustments should be made with PharmD.  
• Combination therapy with daptomycin and ampicillin or ceftaroline may be considered in patients with persistent disease. |
| | Enterococci strains resistant to vancomycin, aminoglycosides, and penicillin | Daptomycin 10-12 mg/kg IV q24h OR Linezolid 600 mg IV/PO q12h | >6 weeks | • Follow baseline and weekly CK with daptomycin therapy.  
• Combination therapy with daptomycin and ampicillin or ceftaroline may be considered in patients with persistent disease. |

**Note:** Cefepime 2 g IV q8h should be used instead of ceftriaxone in burn patients and IV drug users.
### Empiric Therapy

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<th>Duration of Therapy</th>
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<tbody>
<tr>
<td>Staphylococci (MSSA)</td>
<td>Preferred: Oxacillin 2 g IV q4h¹</td>
<td>6 weeks</td>
<td>- Cefazolin should not be used if CNS disease present.</td>
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<tr>
<td></td>
<td>Alternative for PCN Allergy (non-anaphylaxis): Cefazolin 2 g IV q8h³</td>
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<td></td>
<td>Alternative for PCN Allergy (Anaphylaxis): Vancomycin IV⁴</td>
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<tr>
<td>Staphylococci (MRSA)</td>
<td>Preferred: Vancomycin IV⁴</td>
<td>6 weeks</td>
<td>- Follow baseline and weekly CK with daptomycin therapy</td>
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<td></td>
<td>Alternative for Vancomycin Allergy or Failure: Daptomycin 8-10 mg/kg IV q24h¹</td>
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<tr>
<td>HACEK Group</td>
<td>Preferred: Ceftriaxone 2 g IV q24h</td>
<td>4 weeks</td>
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<td></td>
<td>Alternative: Ampicillin-sulbactam 3 g IV q6h¹-³</td>
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<td>Alternative for Severe PCN Allergy: Ciprofloxacin 400 mg IV q8h²</td>
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<td>Candida spp.</td>
<td>Preferred: Liposomal amphotericin B 3-5 mg/kg IV q24h + Flucytosine¹ 25 mg/kg PO q6h</td>
<td>&gt;6 weeks</td>
<td>- Following initial therapy with IV antifungal agent, long-term suppression with an oral azole may be considered for sensitive pathogens.</td>
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<td>Culture negative (acute, presents within days of symptom onset; pending definitive diagnosis)</td>
<td>Vancomycin IV⁴ + Ceftriaxone 2 g IV q24h</td>
<td>4-6 weeks</td>
<td>- Receipt of antibiotics prior to obtaining cultures is the most common cause of culture negative IE. There are many infectious and non-infectious causes. An evaluation of epidemiological factors, history of prior cardiovascular infections, exposure to antimicrobials, clinical course, severity, and extracardiac sites of infection should be performed to help guide diagnosis and treatment.</td>
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<tr>
<td>Culture negative (subacute, presents within weeks of symptom onset; pending definitive diagnosis)</td>
<td>Vancomycin IV⁴ + Ampicillin-sulbactam 3 g IV q6h¹-³ OR Vancomycin IV⁴ + Ceftriaxone 2 g IV q24h</td>
<td>4-6 weeks</td>
<td>- Gentamicin should be added in patients with a high suspicion for Enterococcus infections. Traditional gentamicin dosing (1 mg/kg IV q8h) is preferred, with gentamicin peak goal 3-5 mg/L and trough goal &lt;1 mg/L. In patients with renal insufficiency, dosing adjustments should be made with PharmD. Cefepime 2 g IV q8h¹ should be used instead of ceftriaxone in burn patients and IV drug users for empiric coverage of Pseudomonas.</td>
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</tbody>
</table>

§ Prior to confirmation of pathogen
1. Refer to Antimicrobial Dosing Recommendations for dose adjustments in renal dysfunction
2. If candidate for outpatient therapy, may consider administration via continuous infusion (same daily dose)
3. Please refer to the Aminoglycoside Dosing in Adult Patients for guidance on aminoglycoside dosing.
4. Please refer to the Vancomycin Nomogram for guidance on vancomycin dosing and monitoring.
5. Because of the requirement for frequent dosing and the inability to administer via continuous infusion, these drugs are not recommended for home administration

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**Antimicrobial Subcommittee Approval:** 12/2015  
**Originated:** Unknown

**P&T Approval:** 1/2016  
**Last Revised:** 03/2021

**Revision History:**  
03/21: Updated vancomycin dosing & hyperlinks

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

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