VANDERBILT UNIVERSITY

MEDICAL CENTER

Vanderbilt Adult Antimicrobial Stewardship Program

VUMC Division of Infectious Diseases

# Guidance on Oral Options for Uncomplicated Bacteremia

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**Uncomplicated Bacteremia Definition:**

- Bacteremia originating from one of the following sources:
    - Gastrointestinal/Genitourinary, Intra-abdominal, Central line (removed), Respiratory Tract (without structural lung disease, empyema, or cystic fibrosis), Skin and Soft Tissue
- Source controlled (no hardware or prosthetic involvement) when applicable
- Clinical improvement within 72 hours of antibiotic therapy
- There are no concerns for an endovascular source
- There is no evidence of metastatic sites of infection
- Gram-positive bacteremia clears within 48-72 hours of initiating treatment

**Patient Selection Criteria for PO antimicrobials in Uncomplicated Bacteremia**

To limit PICC Line complications and hospital length of stays, consider a switch to an oral regimen when the following criteria are met:

- ☐ Clinical stability achieved
- ☐ Improvement in signs and symptoms of infection
- ☐ No issues with agent allergies/intolerances
- ☐ No concerns for drug-drug interactions precluding the use of a PO regimen
- ☐ Not morbidly obese (BMI $\geq$ 40) precluding dosing of PO antimicrobial therapy
    - If there are concerns, please speak with ID pharmacy for obesity dosing recommendations
- ☐ Pathogen specific, minimal IV lead in time provided (see below)
- ☐ Susceptibility results support use of the oral antimicrobial
- ☐ Reliable PO intake without comorbidities associated with malabsorption
- ☐ Source controlled infection with cleared cultures for gram-positive infections
- ☐ There are no psychosocial or logistical reasons to prefer IV therapy

This guidance can also be used in the setting of patients discharging against medical advice (AMA). **Durations of therapy may change if extrapolating to other disease states.**

**Antimicrobial Considerations**

| Agent | Bioavailability | Dosing |
|---|---|---|
| Amoxicillin | 70 – 90 % | 1000 mg Q6-8hours |
| Amoxicillin – Clavulanate | 60 – 80 % | 875/125 mg Q8h |
| Cephalexin | 90 - 100 % | 1000 mg Q6h |

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| | | |
|---|---|---|
| Levofloxacin | 99% | 750 mg Q24h |
| Ciprofloxacin | 70 % | 500 mg BID (Enterobacterales)<br>750 mg BID (*Pseudomonas aeruginosa)* |
| Trimethoprim-Sulfamethoxazole (TMP-SMX) | ~100% | 8-12 mg/kg/day of TMP divided Q8-12h |
| Linezolid | ~100% | 600 mg BID |
| Metronidazole | ~100% | 500 mg BID |

**Indications for Repeat Blood Cultures:**

- Uncomplicated Gram-negative bacteremia duration is counted from the first day of active therapy rather than culture clearance. Repeating blood cultures for Gram-negative bacteremia is not routinely done.
- Gram-positive bacteremia duration is determined via culture clearance. Repeating cultures are warranted until clearance is documented.

| **Gram-Negative Pathogens‡** | | | |
|---|---|---|---|
| **Pathogen** | **Susceptibility Driven PO Options** | **Recommended IV Lead Time** | **Uncomplicated Duration** |
| Lactose Fermenting Organisms WITHOUT Chromosomal AmpC | | | |
| *E. coli*<br>*Klebsiella spp.*<br>*P. mirabilis*<br>*C. Koseri* | • Amoxicillin†<br>• Amoxicillin – Clavulanate†<br>• Cephalexin†<br>• Levofloxacin<br>• Ciprofloxacin<br>• TMP-SMX | 72 Hours* | 7 Days |
| Lactose Fermenting Organisms WITH Chromosomal AmpC | | | |
| *E. cloacae*<br>*K. aerogenes*<br>*C. Freundii*<br>*S. Marcescens*<br>*P. vulgaris*<br>*M. Morganii*<br>*Providencia spp.* | • Levofloxacin<br>• Ciprofloxacin<br>• TMP-SMX | - | 7 Days |

| Non-Lactose Fermenting Organisms | | | |
|---|---|---|---|
| *Pseudomonas aeruginosa* | • Levofloxacin<br>• Ciprofloxacin | - | 7 Days |

†Maximum MIC Reliability of 2 mcg/ml

*Does not apply to Fluoroquinolones, TMP-SMX, or Linezolid

‡These durations are for confirmed uncomplicated bacteremia. If extrapolating to patients leaving against medical advice for complicated infections, longer durations are required.

| **Gram-Positive Pathogens‡** | | | |
|---|---|---|---|
| **Pathogen** | **Susceptibility Driven PO Options** | **Recommended IV Lead Time** | **Uncomplicated Duration** |
| Penicillin Susceptible Streptococci | • Amoxicillin<br>• Cephalexin | 72 Hours | 7 Days* |
| | • Levofloxacin<br>• Linezolid | - | |
| Penicillin-intermediate or resistant Streptococci | • Levofloxacin<br>• Linezolid | - | 7 Days* |
| *Enterococcus* Sp. | • Amoxicillin | 7 Days | 7 Days* |
| | • Linezolid | - | |
| Coagulase – Negative *Staphylococcus* | • Linezolid | 72 Hours | 7 Days* |

*Consider 14 days of therapy in patients who do not respond quickly clinically, have delayed clearance, or patients who have a source of infection that is not intervened on.

‡These durations are for confirmed uncomplicated bacteremia. If extrapolating to patients leaving against medical advice for complicated infections, longer durations are required.

| **Uncomplicated* *Staphylococcus aureus* bacteremia‡** | | | |
|---|---|---|---|
| **Pathogen** | **Susceptibility Driven PO Options** | **Recommended IV Lead Time** | **Uncomplicated Duration** |
| *S. aureus* | • Linezolid<br>• TMP-SMX | 7 Days † | 14 Days |

*Data regarding oral antimicrobials for *S. Aureus* bacteremia (SAB) is limited. These recommendations are primarily based on the results of the SABATO and POET trial. SABATO trial excluded patients with endocarditis, pneumonia, infected implants, osteomyelitis, undrained abscesses, septic shock ,bacteremia for > 72 hours, recurrent bacteremia, severe immunodeficiency, prosthetic heart valves, injection drug use, or vascular grafts. The POET trial focused on patients with native valve endocarditis and did not contain patients with MRSA bacteremia. **Patients should be evaluated carefully for consideration of PO therapy for SAB to ensure they are source controlled, stable, have reliable absorption, and are not persistently bacteremic.**

† Despite the high bioavailability of these agents, data is currently lacking to support initial therapy with enteral options. An IV lead in time with more traditional agents (vancomycin, cefazolin, etc. ) is recommended before considering a PO step down option.

‡These durations are for confirmed uncomplicated bacteremia. If extrapolating to patients leaving against medical advice for complicated infections, longer durations are required.

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