Lefamulin Activity against a Contemporary Global Collection of Staphylococcus aureus

INTRODUCTION

- Lefamulin is a first-in-class, oral, IV pleuromutilin antibiotic approved in the United States (US), Europe (EU), and Canada for the treatment of community-acquired pneumonia (CAP) in adults caused by susceptible typical and atypical bacterial organisms, including S. aureus.
- Susceptibility testing was performed by CLSI broth microdilution reference methods and EUCAST breakpoints were used.

RESULTS

- Lefamulin was highly active against the S. aureus collection across all geographic regions (MIC\text{\textsubscript{\text{50}}} ≤ 0.06 mg/L with 99.3% of isolates inhibited at ≤0.25 mg/L, consistent with the susceptible breakpoint published by EUCAST and CLSI (Table 1 and Figure 2 to 4).
- Limited variation, no more than 1 log, dilution, was observed in lefamulin MIC\text{\textsubscript{\text{50}}} values for all regions (data not shown).
- Lefamulin was active against methicillin-resistant (R) S. aureus (MRSA), with an MIC\text{\textsubscript{\text{50}}} of ≤0.06 mg/L and ≥99.3% susceptibility (Table 1 and Figures 2 and 3).
- Lefamulin activity was unaffected by other resistance phenotypes, such as (Table 1 and Figure 4):
  - Antibiotic-nonsusceptible (NS): MIC\text{\textsubscript{\text{50}}} of ≤0.06 mg/L and ≥99.7% S;
  - Methicillin-R: MIC\text{\textsubscript{\text{50}}} of ≤0.25 mg/L and ≥98.5% S;
  - Chloramphenicol-NS: MIC\text{\textsubscript{\text{50}}} of ≤0.12 mg/L and ≥98.0% S;
  - Doxycycline-NS: MIC\text{\textsubscript{\text{50}}} of ≤0.06 mg/L and ≥98.5% S;
  - Gentamicin-R: MIC\text{\textsubscript{\text{50}}} of ≤0.25 mg/L and ≥98.5% S;
  - Trimethoprim-sulfamethoxazole-NS: MIC\text{\textsubscript{\text{50}}} of ≤0.06 mg/L and ≥100.0% S;
- MRSA susceptibilities to azithromycin, ceftriaxone, and moxifloxacin were 24.2%, 90.5%, and 38.9%, respectively.

CONCLUSIONS

- Lefamulin demonstrated potent in vitro antibacterial activity against S. aureus including MRSA collected from patients worldwide regardless of geographic region and resistance phenotype.
- Lefamulin represents a valuable empiric treatment option for ambulatory and hospitalized patients with CAP, including those infected with S. aureus.
- Further studies are warranted to investigate the efficacy of lefamulin in other S. aureus infections.

Figure 2. Antimicrobial susceptibility of S. aureus collected worldwide (2020–2021)

Figure 3. Antimicrobial susceptibility of MRSA isolates collected worldwide (2020–2021)

Figure 4. Lefamulin activity (cumulative MIC distributions) against S. aureus resistant subsets

Table 1. Antimicrobial susceptibility of S. aureus stratified by phenotype

<table>
<thead>
<tr>
<th>Resistant subset (no.)</th>
<th>Lefamulin</th>
<th>Azithromycin</th>
<th>Ceftriaxone</th>
<th>Moxifloxacin</th>
<th>Linezolid</th>
<th>Vancomycin</th>
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<tbody>
<tr>
<td>MRSA, all (n=13,911)</td>
<td>≤0.25 (93.3)</td>
<td>1 ≤ 24 (24.2)</td>
<td>≤0.06 (91.8)</td>
<td>2 ≤ 100 (38.5)</td>
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<td>MRSA-NS (n=13,711)</td>
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<td>S. aureus (n=9,528)</td>
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Abbreviations: A2I, azithromycin; DOX, doxycycline; MXX, moxifloxacin; LZD, linezolid; TMP-SMX, trimethoprim-sulfamethoxazole; CPT, ceftriaxone; VAN, vancomycin.

MRSA rates (% susceptible)

- 0–45: 10.0–45.0%
- 45–55: 5.0–55.0%
- ≥55: ≥55.0%

REFERENCES


Table 1. Susceptibility of S. aureus selected for the SENTRY Program (n=13,911 isolates; 2020–2021)

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