**02033 | 02033 *In Vitro* Activity of Lefamulin against Bacterial Pathogens causing Pneumonia and Other Respiratory Tract Infections in Europe: Results from the SENTRY Surveillance Program (2019-2020)**

# 02. Bacterial infection & disease

2c. Community-acquired respiratory infections

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**Background** Lefamulin (Xenleta™) is the first-in-class pleuromutilin protein synthesis inhibitor recently approved for IV and oral treatment of community-acquired pneumonia (CAP). Lefamulin IV or IV/oral (5–7 days; 10 days for methicillin-resistant Staphylococcus aureus [MRSA]) and lefamulin oral (5 days) regimens were noninferior to moxifloxacin IV or IV/oral (7 days; 10 days for MRSA) and moxifloxacin oral (7 days) in patients with CAP caused by the most prevalent typical and atypical bacterial pathogens. This study investigated the in vitro activity of lefamulin and comparators against bacterial respiratory pathogens collected from European medical centers in 2019-2020.

**Methods** 1,711 organisms (1/patient) were collected from 36 medical centers in 19 European countries from patients with community-acquired respiratory tract infections and from pneumonia in hospitalized patients. Lefamulin and comparators were tested by CLSI broth microdilution methods. EUCAST breakpoints (2021) were applied for lefamulin and comparators.

**Results** Lefamulin was highly active against S. pneumoniae (Table). Only 1 isolate was lefamulin-nonsusceptible (NS), with a lefamulin MIC of 1 mg/L (susceptible [S] at ≤0.5 mg/L). Moxifloxacin (99.4%S) was also very active against S. pneumoniae; whereas amoxicillin/clavulanate and ceftriaxone were active against 83.3% and 86.1% of isolates, respectively. Only 77.4% of S. pneumoniae isolates were azithromycin-susceptible. Lefamulin retained potent activity against penicillin-resistant (penicillin MIC >2 mg/L), azithromycin-resistan (azithromycin MIC >0.5 mg/L), and tetracycline-resistant (tetracycline MIC >2 mg/L). Lefamulin was also very active against S. aureus (MIC50/90, 0.06/0.12 mg/L; 100.0%S), including MRSA isolates (MIC50/90, 0.06/0.12 mg/L; 100.0%S) and other resistant subsets. Among H. influenzae, lefamulin displayed potent activity (MIC50/90 of 0.5/2 mg/L) with 99.4% of isolates, including 100.0% of β-lactamase-positive isolates, inhibited at the US FDA susceptible breakpoint of ≤2 mg/L. M. catarrhalis isolates, which were mostly β-lactamase-positive (97.5%), were highly susceptible to lefamulin (MIC50/90, 0.06/0.12 mg/L; highest MIC, 0.5 mg/L).

**Conclusions** Lefamulin demonstrated potent in vitro activity against contemporary bacteria collected from patients with pneumonia in European medical centres. Lefamulin activity was not adversely affected by resistance to other antimicrobial classes, including β-lactams, macrolides, fluoroquinolones, and tetracyclines. Lefamulin represents a valuable empiric treatment option for outpatients and hospitalized patients with CAP in Europe.

Table

Table. Antimicrobial activity of lefamulin and comparators against bacterial isolates causing pneumonia in Europe (2019-2020)

| | $MIC_{50/90}$ in mg/L (% susceptible per EUCAST criteria) | | | | | |
|---|---|---|---|---|---|---|
| **Organism (no. of isolates)** | **Lefamulin** | **Amox/Clav** | **Azithromycin** | **Tetracycline** | **Moxifloxacin** | **Ceftriaxone** |
| *S. pneumoniae* (958) | 0.12/0.25 (99.9) | ≤0.03/2 (83.3) | 0.12/>4 (77.4) | 0.25/>4 (81.4) | 0.12/0.25 (99.4) | 0.03/1 (86.1) |
| Penicillin-resistant (54)[a] | 0.06/0.12 (100.0) | >4/>4 (0.0) | >4/>4 (37.0) | >4/>4 (44.4) | 0.12/0.25 (100.0) | 1/2 (0.0) |
| Azithromycin-resistant (191) | 0.06/0.12 (99.5) | 0.5/4 (50.3) | >4/>4 (0.0) | >4/>4 (23.0) | 0.12/0.25 (97.4) | 0.5/2 (58.6) |
| Tetracycline-resistant (171) | 0.06/0.12 (100.0) | 0.5/4 (50.9) | >4/>4 (7.6) | >4/>4 (0.0) | 0.12/0.25 (98.2) | 0.5/2 (57.3) |
| *H. influenzae* (322) | 0.5/2 (99.4) | 0.5/2 (97.5) | 1/1 (98.1) | 0.5/0.5 (99.1) | 0.03/0.06 (96.6) | 0.004/0.015 (99.7) |
| β-lactamase-positive (46) | 0.5/1 (100.0) | 1/2 (95.7) | 0.5/1 (100.0) | 0.5/0.5 (95.7) | 0.03/0.06 (95.7) | 0.004/0.008 (100.0) |
| *M. catarrhalis* (240) | 0.06/0.12 [a] | 0.12/0.25 (100.0) | 0.03/0.03 (99.6) | 0.25/0.5 (100.0) | 0.06/0.06 (100.0) | 0.25/0.5 (99.2) |
| *H. parainfluenzae* (15) | 1/2 [b] | 0.5/2 (100.0) | 1/1 (100.0) | 0.5/1 (100.0) | 0.06/0.25 (66.7) | 0.004/0.15 (100.0) |
| *S. aureus* (176) | 0.06/0.12 (100.0) | Not Tested | 0.5/>8 (63.1) | ≤0.5/≤0.5 (90.9) | ≤0.06/2 (83.5) | Not Tested |
| MRSA (30) | 0.06/0.12 (100.0) | Not Tested | >8/>8 (30.0) | ≤0.5/>8 (76.7) | 1/4 (40.0) | Not Tested |
| Azithromycin-resistant (61) | 0.06/0.12 (100.0) | Not Tested | >8/>8 (0.0) | ≤0.5/>8 (83.6) | ≤0.06/2 (68.9) | Not Tested |
| Moxifloxacin-resistant (29) | 0.06/0.12 (100.0) | Not Tested | >8/>8 (31.0) | ≤0.5/2 (89.7) | 2/4 (0.0) | Not Tested |
| Ceftaroline-resistant (12) [c] | 0.06/0.12 (100.0) | Not Tested | >8/>8 (16.7) | ≤0.5/≤0.5 (91.7) | 2/4 (0.0) | Not Tested |

[a] Penicillin MIC of >2 mg/L (other than meningitis). [b] Breakpoints have not been established. [c] EUCAST pneumonia breakpoint of >1 mg/L was applied.

**Keyword 1**
Pleuromutilin
**Keyword 2**
Streptococcus pneumoniae
**Keyword 3**
MRSA

## Conflicts of interest

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