In Vitro Activity of Ceftobiprole and Comparator Agents Against Contemporary US Clinical Isolates Collected in 2025 Following FDA Approval

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Background

- Ceftobiprole is an intravenous cephalosporin with activity against clinically important Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), and selected Gram-negative and respiratory pathogens.
- The US FDA approved ceftobiprole in April 2024 for adults with *S. aureus* bacteremia, including right-sided infective endocarditis; adults with acute bacterial skin and skin structure infections (ABSSSI); and adult and pediatric patients with community-acquired bacterial pneumonia (CABP) caused by susceptible isolates (Table 2).
- Post-approval surveillance provides ongoing assessment of antimicrobial activity against contemporary U.S. clinical isolates and enables detection of potential changes in susceptibility patterns following clinical introduction.

Methods

Bacterial isolates

- A total of 4,126 clinical isolates were collected from 31 US medical centers across all 9 US census divisions during 2025 as part of the SENTRY Antimicrobial Surveillance Program (Figure 1).
- Isolates were primarily recovered from hospitalized patients with bloodstream infections (BSI; 45%), ABSSSI (20%), and respiratory tract infections (35%).

Susceptibility testing

- Isolates were tested for susceptibility by broth microdilution according to CLSI approved methods using cation-adjusted Mueller–Hinton broth (CAMHB).
- CLSI and FDA (for ceftobiprole) breakpoint criteria were applied for interpretation of MIC results. *E. coli* and *K. pneumoniae* displaying MIC results ≥2 mg/L for aztreonam or ceftazidime or ceftriaxone were defined as presumptive extended-spectrum β-lactamase (ESBL) producers.

Results

- Against 1,606 *S. aureus* isolates, ceftobiprole demonstrated $MIC_{50/90}$ values of 0.5/1 µg/mL, and 99.7% susceptibility overall, including susceptibility against 100% of MSSA and 99.2% of MRSA isolates (Table 1 and Figure 2).
- Among the subset of *S. aureus* isolates recovered from BSI (n = 553) and ABSSSI (n = 548), ceftobiprole susceptibility remained high (99.1–100% susceptible) (Table 2).
- When tested against 199 β-hemolytic streptococci, ceftobiprole inhibited all isolates at an MIC of ≤0.03 µg/mL ($MIC_{50/90}$, 0.008/0.03 µg/mL), whereas the ceftobiprole $MIC_{50/90}$ values against Viridans group streptococci (VGS) were 0.06/0.25 µg/mL (Table 1).
- Among respiratory pathogens, ceftobiprole demonstrated activity against *S. pneumoniae* and *H. influenzae*, with $MIC_{50/90}$ values of 0.008/0.25 µg/mL and 0.03/0.12 µg/mL, respectively; susceptibility rates were 98.8% and 97.8%, respectively (Table 1).
- As expected, ceftobiprole demonstrated limited activity against presumed ESBL-producing isolates, whereas ceftobiprole retained activity against non-ESBL *E. coli* and *K. pneumoniae*, with susceptibility rates of 100% and 99.7%, respectively (Table 1).

Conclusions

- Ceftobiprole demonstrated potent in vitro activity against contemporary U.S. clinical isolates collected in 2025, including pathogens associated with all current FDA-approved indications.
- Against 1,606 *S. aureus* isolates, ceftobiprole remained highly active, with susceptibility rates of 99.7% overall, including 100% of MSSA and 99.2% of MRSA isolates.
- Ceftobiprole also demonstrated potent activity against β-hemolytic streptococci, *S. pneumoniae*, and *H. influenzae*, supporting continued activity against pathogens relevant to ABSSSI and CABP indications.
- Among Enterobacterales, ceftobiprole retained activity against presumed non-ESBL *E. coli* and *K. pneumoniae* isolates but showed limited activity against presumed ESBL-producing isolates, consistent with its expected antibacterial spectrum.
- These findings establish an important post-approval benchmark for ceftobiprole activity in the United States and provide a foundation for longitudinal surveillance of susceptibility trends during the ongoing monitoring program.

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Figure 1. Geographic representation of the U.S. ceftobiprole surveillance program. A total of 4,126 contemporary clinical isolates were collected from 31 participating medical centers representing all 9 U.S. Census divisions. The surveillance collection included pathogens recovered from bloodstream, respiratory tract, and skin and skin structure infections and was designed to provide a geographically representative assessment of ceftobiprole activity in the United States.

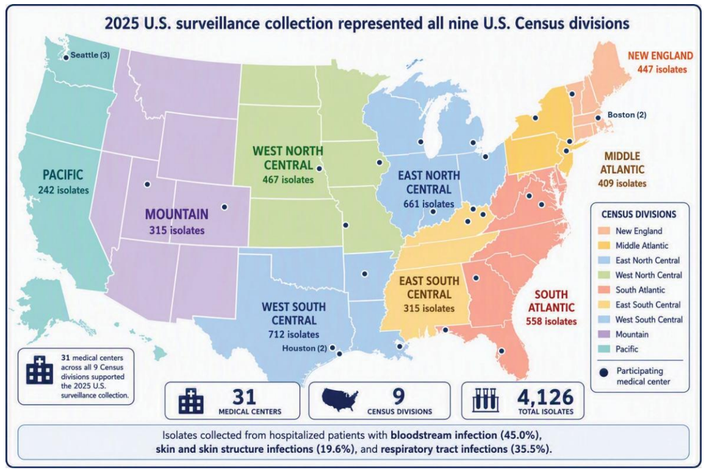


Figure 2. Activity of ceftobiprole against contemporary MSSA and MRSA isolates collected in the US. MIC distributions demonstrate sustained *in vitro* activity against both MSSA and MRSA, with susceptibility rates of 100% and 99.2%, respectively. Although MRSA isolates exhibited a modest shift toward higher MIC values than MSSA isolates, the overwhelming majority remained at or below the FDA susceptible breakpoint (≤2 µg/mL).

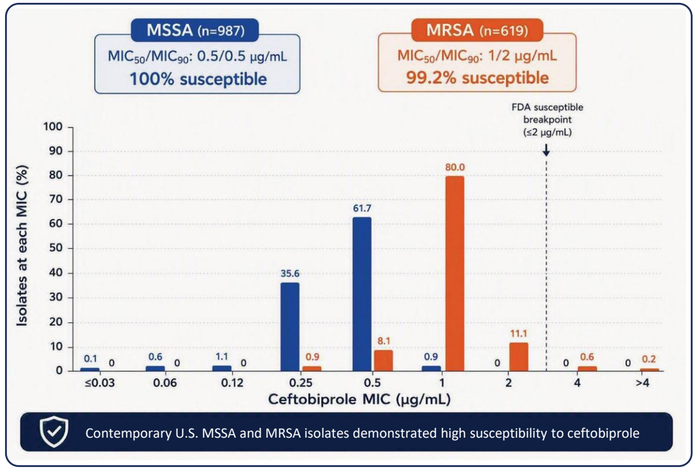


Table 1. Activity of ceftobiprole and comparator agents against surveillance clinical isolates collected from US sites in 2025

Species/group (No. tested)	MIC_{50}/MIC_{90} in mg/L (% susceptible by CLSI/FDA)[a]						
	BPR	**CPT**	**CLI**	**CRO**	**DAP**	**LZD**	**VAN**
S. aureus (1,606)	0.5/1 (99.7)	0.25/1 (98.6)	0.06/>2 (89.4)	4/>8 (61.5)[b]	0.25/0.25 (99.9)	1/2 (100)	1/1 (100)
Methicillin-susceptible (987) [b]	0.5/0.5 (100)	0.25/0.25 (100)	0.06/0.12 (96.9)	4/4 (100)[b]	0.25/0.25 (100)	1/2 (100)	1/1 (100)
Methicillin-resistant (619) [b]	1/2 (99.2)	0.5/1 (96.4)	0.06/>2 (77.4)	>8/>8 (0.0)[b]	0.25/0.25 (99.8)	1/2 (100)	1/1 (100)
	BPR	**CPT**	**A/C**	**AZI**	**CRO**	**LEV**	**PEN**
β-hemolytic streptococci (199) [c]	0.008/0.03 (100)	≤0.008/0.015 (100)	≤0.03/0.06 (100)	0.12/>4 (54.8)	0.03/0.06 (100)	0.5/1 (99.0)	0.015/0.06 (100)
Viridans group streptococci (96) [d]	0.06/0.25 (—)	0.015/0.06 (—)	0.12/1 (—)	2/>4 (42.1)	0.12/0.5 (96.9)	1/>4 (75.0)	0.12/1 (57.3)
S. pneumoniae (406)	0.008/0.25 (98.8)	≤0.008/0.12 (100)	≤0.03/2 (96.8)	0.06/>4 (59.5)	0.015/0.5 (98.0)	1/1 (100)	0.015/2 (96.3)
H. influenzae (182)	0.03/0.12 (97.8)	0.008/0.03 (100)	0.5/2 (93.4)	1/2 (97.3)	0.004/0.015 (100)	0.015/0.03 (98.9)	1/>4 (—)
	BPR	**A/C**	**CRO**	**IMI**	**P/T**	**LEV**	**GEN**
E. coli (807)	0.03/>16 (73.0)	8/32 (73.0)	≤0.06/>8 (72.4)	0.12/0.25 (99.5)	2/8 (92.7)	0.06/16 (67.4)	0.5/>16 (85.5)
Non-ESBL (560)	0.03/0.06 (100)	8/16 (83.6)	≤0.06/0.12 (100)	0.12/0.12 (100)	2/4 (97.5)	0.03/8 (82.5)	0.5/2 (91.2)
ESBL (247)	>16/>16 (11.7)	16/32 (49.0)	>8/>8 (9.7)	0.12/0.25 (98.4)	4/32 (81.8)	8/32 (33.2)	1/>16 (72.5)
K. pneumoniae (541)	0.03/>16 (73.0)	2/16 (78.6)	≤0.06/>8 (74.9)	0.12/0.25 (97.0)	4/32 (79.1)	0.06/4 (83.5)	0.25/>16 (87.8)
Non-ESBL (388)	0.03/0.06 (99.7)	2/8 (96.4)	≤0.06/0.12 (100)	0.12/0.25 (100)	4/8 (92.3)	0.06/0.25 (95.9)	0.25/0.5 (98.7)
ESBL (153)	>16/>16 (5.2)	16/32 (33.3)	>8/>8 (11.1)	0.12/2 (89.5)	16/>128 (45.8)	0.5/16 (52.3)	0.25/>16 (60.1)

BPR, ceftobiprole; CPT, ceftaroline; CLI, clindamycin; CRO, ceftriaxone; DAP, daptomycin; LZD, linezolid; VAN, vancomycin; A/C, amoxicillin-clavulanate (2:1 ratio); AZI, azithromycin; LEV, levofloxacin; PEN, parenteral penicillin; IMI, imipenem; P/T, piperacillin-tazobactam; GEN, gentamicin; ESBL, extended-spectrum β-lactamase; *E. coli* and *K. pneumoniae* displaying MIC results ≥2 mg/L for aztreonam or ceftazidime or ceftriaxone were defined as presumptive ESBL producers, whereas those with MIC results <2 mg/L for aztreonam and ceftazidime and ceftriaxone were defined as presumptive non-ESBL producers.
[a] Percentage susceptible results for ceftobiprole according to the respective breakpoints approved by the FDA, including susceptible breakpoint for *S. pyogenes* applied to β-hemolytic streptococci. Susceptibility to comparator agents determined based on CLSI breakpoints. "—" breakpoint not available.
[b] Methicillin-susceptible and -resistant *S. aureus* isolates using oxacillin as a surrogate agent. Ceftriaxone susceptibility against *S. aureus* determined based on the oxacillin results used as a surrogate.
[c] *Streptococcus agalactiae* (79), *S. canis* (2), *S. dysgalactiae* (20), *S. equi* (1), and *S. pyogenes* (97).
[d] *Streptococcus anginosus* group (10), *S. constellatus* (4), *S. equinus* group (2), *S. gallolyticus* (4), *S. gordonii* (5), *S. intermedius* (4), *S. mitis* group (48), *S. mitis/oralis* (2), *S. mutans* (2), *S. parasanguinis* (5), *S. salivarius* group (4), *S. sanguinis* (5), and *S. vestibularis* (1).

Table 2. Ceftobiprole FDA-approved indications and *in vitro* activity against current indicated pathogens

Approved indication	Indicated pathogens	Ceftobiprole susceptibility in indication-specific isolate subsets (n)
S. aureus bacteremia, including right-sided infective endocarditis (adult)	MSSA and MRSA	*S. aureus*: **99.6% susceptible** (n = 553) MSSA: **100% susceptible** (n = 325) MRSA: **99.1% susceptible** (n = 228)
Acute bacterial skin and skin structure infections (adult)	MSSA, MRSA, and β-hemolytic streptococci	*S. aureus*: **100% susceptible** (n = 548) MSSA: **100% susceptible** (n = 346) MRSA: **100% susceptible** (n = 202) β-hemolytic streptococci: **100% susceptible** (n = 81)
Community-acquired bacterial pneumonia (adult and pediatric)	*S. pneumoniae* and *H. influenzae*	*S. pneumoniae*: **98.9% susceptible** (n = 355) *H. influenzae*: **97.8% susceptible** (n = 182)

References

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ZEVTERA Prescribing Information (ceftobiprole medocaril sodium; injection for intravenous use). Available at https://zevtera-assets.s3.amazonaws.com/prescribing-information.pdf.