

30 September 2024

CLSI Investigational Use-Only Breakpoints

Although investigational breakpoints are published in the current edition of CLSI M100,¹ a revision to CLSI M23² required that investigational breakpoints not be included in future editions of CLSI M100.¹ The following susceptible-only breakpoints were established using *in vitro* susceptibility testing on contemporary global resistant isolates, *in vivo* mouse model data, and pharmacokinetic and pharmacodynamic data paired with models to achieve efficacy against carbapenem-resistant isolates and are considered investigational use only. Antimicrobial susceptibility testing by disk diffusion or agar dilution was not reviewed. Therefore, breakpoints are provided only for cation-adjusted Mueller-Hinton broth (CAMHB).

Table 1. Zone Diameter and MIC Breakpoints for Cefepime-Zidebactam

Testing Conditions	Routine QC Recommendations
Cefepime-zidebactam in a fixed 1:1 ratio	
Medium: Broth dilution: CAMHB	<i>Acinetobacter baumannii</i> NCTC 13304
Inoculum: Broth culture method or colony suspension, equivalent to a 0.5 McFarland standard	When a commercial test system is used for susceptibility testing, refer to the manufacturer's instructions for QC test recommendations and QC ranges.
Incubation: 35°C ± 2°C; ambient air Dilution methods: 16–20 hours	

Organism	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL			
		S	SDD	I	R	S	SDD	I	R
CEFEPIME-ZIDEACTAM									
The breakpoints were based on <i>in vitro</i> susceptibility testing on contemporary global resistant isolates, <i>in vivo</i> mouse model data, and pharmacokinetic and pharmacodynamic data from healthy volunteers paired with models to achieve efficacy against carbapenem-resistant isolates. No clinical data were available to inform these breakpoints.									
Enterobacterales	-	-	-	-	-	≤ 64/64	-	-	-
<i>Pseudomonas aeruginosa</i>	-	-	-	-	-	≤ 64/64	-	-	-
<i>Acinetobacter baumannii</i>	-	-	-	-	-	≤ 64/64	-	-	-

Abbreviations: CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MIC, minimal inhibitory concentration; NCTC, National Collection of Type Cultures; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent.

References for Table 1

¹ CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 34th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2024.

² CLSI. *Development of In Vitro Susceptibility Test Methods, Breakpoints, and Quality Control Parameters*. 6th ed. CLSI guideline M23. Clinical and Laboratory Standards Institute; 2023.