Click to prove you're human

The Clinical and Laboratory Standards Institute (CLSI) Subcommittee on Antimicrobial Susceptibility Testing convened meetings in January and June 2024 to discuss several key updates, including revised breakpoint ranges and the introduction of new breakpoints by ad hoc working groups (AHWGs). These changes aim to improve clinical care by making carbapenemase testing more accessible and efficient. Several concerns were highlighted regarding the current definition of carbapenem-resistant Enterobacterales (CRE), which can lead to unnecessary testing in isolates unlikely to produce carbapenases. To address this, data from various sources, including the JMI Laboratories SENTRY Antimicrobial Surveillance Program, was analyzed to determine the sensitivity and specificity of different criteria for identifying CRE. The study revealed that relying solely on meropenem resistance would miss approximately 10% of Klebsiella pneumoniae carbapenemase (KPC)-producing isolates and more than 40% of OXA-48-like isolates. Therefore, a revised definition was proposed, stating that isolates resistant to any carbapenem tested, except for specific exceptions, should undergo carbapenemase testing using phenotypic or molecular assays. Furthermore, the CLSI updated its guidelines to include new investigational breakpoints for cefepime/zidebactam susceptibility testing. These changes aim to facilitate the analysis of clinical trial data and improve the interpretation of surveillance MIC results.ampicillin/sulbactam (fep/zid) breakpoints for various gram-negative bacteria, including Acinetobacter baumannii ---------- The fep/zid MIC method has been approved by CLSI and the European Committee on Antimicrobial Susceptibility Testing, with MICs determined at a 1:1 ratio of fep and zid. Bacterial efficacy of fep/zid was demonstrated in plasma human-simulated regimens for A baumannii lung and thigh infections. table 2 | pathogen | n | mic90 | | --- | --- | --- | | P. aeruginosa | 1413 | 8-16 µg/mL | | CRAB | 1488 | 32-64 µg/mL | The AHWG acknowledged the fep/zid MIC breakpoint as investigational, with uncertainty in the range of 32 to 64 µg/mL for P. aeruginosa. ampicillin/sulbactam breakpoints Ampicillin/sulbactam (AMP-SUL) is recommended as first-line treatment for CRAB due to its unique intrinsic antibacterial activity against Acinetobacter through inhibition of penicillin-binding protein (PBP)-3 and PBP-1. susceptible breakpoint The estimated ECOFF/ECV using data sets supported the current susceptible breakpoint at 8/4 µg/mL. However, multiple PK/pharmacodynamic studies reported that no dosing regimens were sufficient for SUL MIC greater than 16 µg/mL with low probability of target attainment (PTA). clinical data Clinical data were largely uninformative for breakpoint reevaluation, but the dose (1 g every 6 hours as an extended infusion given over ≥ 3 hours) on which the breakpoint is based will be added to the 35th edition of the M100. minocycline Minocycline is a second-generation tetracycline that binds the 30S ribosomal subunit, inhibiting protein synthesis. It is FDA approved for infections caused by Acinetobacter, including CRAB and extensively drug-resistant strains. An estimated ECOFF of 0.5 µg/mL was established using 2013-2022 SENTRY data. dosing recommendations Approved adult dosing for the intravenous formulation of minocycline is one 200-mg dose followed by 100 mg every 12 hours, with a maximum dose of 400 mg in 24 hours (eg, 200 mg every 12 hours).The current MIC breakpoints for minocycline have been revised to less than or equal to 1 µg/mL, with doses of 200 mg every 12 hours being recommended for susceptible isolates. The revised breakpoints are based on dosing and clinical outcomes data, which demonstrated insufficient evidence to support the previous breakpoints. The revised MIC breakpoints are as follows: ≤ 1 µg/mL (susceptible), 2 µg/mL (intermediate), and ≥ 4 µg/mL (resistant). ========== Looking at recent research on Acinetobacter baumannii infections, it appears that multiple studies have focused on the pharmacokinetics and pharmacodynamics of various antibiotics, including sulbactam. Researchers such as Yokoyama et al., Housman ST et al., and O'Donnell JP et al., have investigated dosing considerations for Acinetobacter baumannii infections in patients with impaired renal function. For instance, a study published by Yokoyama et al. analyzed population pharmacokinetic-pharmacodynamic target attainment analysis of sulbactam in patients with impaired renal function. Similarly, O'Donnell JP et al. investigated the pharmacokinetics/pharmacodynamic relationship of durlobactam in combination with sulbactam. Additionally, researchers like Setiawan E et al. and Cotta MO et al., have conducted population pharmacokinetics and dosing simulations of ampicillin and sulbactam in hospitalized adult patients. Another study by Jaruratanasirikul S et al. aimed to optimize dosage regimens of sulbactam in critically ill patients with severe sepsis caused by Acinetobacter baumannii. Minocycline has also been studied for its effectiveness against multidrug-resistant Acinetobacter infections, as highlighted in a review by Ritchie DJ and Garavaglia-Wilson A. Flamm RK et al. investigated the in vitro activity of minocycline against various bacterial pathogens, including U.S. isolates of Acinetobacter baumannii-Acinetobacter calcoaceticus species complex. Furthermore, researchers have emphasized the importance of antimicrobial susceptibility test results and developed modernized Acinetobacter baumannii susceptibility test interpretive criteria using pharmacometric approaches. Studies like Lodise TP et al. and Goff DA et al., have also explored the pharmacokinetic and pharmacodynamic profiling of minocycline for injection. Overall, these studies suggest that a better understanding of the pharmacokinetics and pharmacodynamics of antibiotics can lead to improved treatment strategies for Acinetobacter baumannii infections.The latest edition of CLSI M100-Ed35 supersedes CLSI M100-Ed34, published in **2024**. Notable updates include new tables, revised content, and **boldfaced changes** indicating significant alterations since the previous version. Major additions to CLSI M100-Ed35 are summarized below, with further details provided by section/table. Users should replace previously published tables with these updated tables to ensure accuracy in their documentation. Key changes to the document include: * Updated product details and print codes * Revised organization of instructions for use * Acknowledgement from the U.S. Food and Drug Administration (FDA) as an approved-level consensus standard It is essential to utilize the latest edition, as **outdated documents are strongly discouraged**. CLSI M100-Ed35 offers 428 pages in print format and 428 pages in PDF format. The document has been accredited by ANSI and serves as a globally recognized standard for AST interpretive criteria.