

WayScience

An abstract graphic featuring a large, swirling shape. The swirl starts with a light blue outer edge, transitions into a darker blue inner ring, and then curves into a bright pink outer edge. The background is a light blue gradient.

2nd International Scientific
and Practical Internet Conference

«Progressive Opportunities and
Solutions of Advanced Society»

ISBN 978-617-8293-36-9

WayScience

2nd International Scientific
and Practical Internet Conference

«Progressive Opportunities and
Solutions of Advanced Society»

ISBN 978-617-8293-36-9

Editorial board of International Electronic Scientific and Practical Journal «WayScience»
(ISSN 2664-4819 (Online))

The editorial board of the Journal is not responsible for the content of the papers and may not share the author's opinion.

**Progressive Opportunities and Solutions of Advanced Society:
Proceedings of the 2nd International Scientific and Practical Internet
Conference, November 7-8, 2024. FOP Marenichenko V.V., Dnipro, Ukraine,
311 p.**

ISBN 978-617-8293-36-9

2nd International Scientific and Practical Internet Conference "Progressive Opportunities and Solutions of Advanced Society" is devoted to research and discussion in various aspects of modern world development.

Topics cover all sections of the International Electronic Scientific and Practical Journal "WayScience", namely:

- public administration sciences;
- philosophical sciences;
- economic sciences;
- historical sciences;
- legal sciences;
- agricultural sciences;
- geographic sciences;
- pedagogical sciences;
- psychological sciences;
- sociological sciences;
- political sciences;
- philological sciences;
- technical sciences;
- medical sciences;
- chemical sciences;
- biological sciences;
- physical and mathematical sciences;
- other professional sciences.

Dnipro, Ukraine – 2024

REVIEW OF NEW FIXED COMBINATIONS OF ANTIBIOTICS IN THE FIGHT AGAINST SUPERINFECTION

Doroshenko O.M.

Assistant of the Department of Pharmacology and Medical Prescription
Kharkiv National Medical University
+380950245290
om.doroshenko@kmmu.edu.ua

Resistance of gram-negative bacteria to antimicrobial drugs has increased exponentially globally in recent years and is a daily challenge for hospital practice. The irrational choice of antimicrobial drugs, their dosage regimens, and the coronavirus pandemic cause therapeutic failures and lead to the further escalation of antimicrobial resistance. [1, p. 5] An extremely relevant way to limit its spread is using already-known antibiotics in combination with beta-lactamase inhibitors. During the current year, the European Medicines Agency (EMA) approved two new drugs that are a combination of a beta-lactam antibiotic and a beta-lactamase inhibitor - cefepime/enmetazobactam and aztreonam/avibactam. Both drugs are positioned for treating complicated urinary tract infections, including pyelonephritis, and nosocomial pneumonia, including those associated with mechanical ventilation. [2]

The purpose of the work was a theoretical study of the features and generalisation of information about new fixed combinations of antibacterial drugs and the determination of the following directions of scientific research.

The official reports of the European Medicines Agency (EMA), European Committee on Antimicrobial Susceptibility Testing (EUCAST) protocols, the PubMed platform, and the MSD directory were processed for analysis. Theoretical methods of research - analysis, synthesis and generalisation - were used.

The mechanism of action of cefepime and aztreonam, due to their belonging to beta-lactam antibiotics, is inhibition of final transpeptidation due to the formation of covalent bonds with penicillin-binding proteins that have transpeptidase and carboxypeptidase activity, thus preventing the formation of cross-links peptidoglycan. [3]

The pharmacodynamic advantage of cefepime includes the development of a bactericidal effect by triggering autolytic enzymes in the bacterial envelope. Its spectrum of action includes gram-positive cocci, gram-negative bacilli (enhanced activity), in particular *P. aeruginosa*, as well as some species of *Enterobacteriales* that produce AmpC beta-lactamase in specific species of *Enterobacter*. [4]

Aztreonam is the only beta-lactam antibiotic that exhibits resistance to enzymes, including Metallo- β -lactamase (MBL)-producing bacteria. Still, monobactams are cleaved by other β -lactamases often co-produced with MBL, limiting the clinical utility of aztreonam monotherapy. Its spectrum of action includes *Enterobacteriales* that do not produce AmpC beta-lactamase, extended-spectrum beta-lactamase (ESBL) or carbapenemase *Klebsiella pneumoniae* (KPC) and *P. aeruginosa*. [5]

Compared to single-component drugs, combinations with beta-lactamase inhibitors show extraordinary resistance to developing resistance. Cefepime/enmetazobactam is a fixed-dose combination of the intravenous antibiotic enmetazobactam, a novel extended-spectrum lactamase inhibitor belonging to the penicillanic acid sulfone class, with the 4th-generation cephalosporin cefepime. EMA evaluation reports show that enmetazobactam restores the efficacy of cefepime against some multidrug-resistant bacteria, including ESBL-producing pathogens, alone or in combination with some beta-lactamase resistance mutations, such as OXA-48 or AmpC, which are on the rise in Europe and for which there are few therapeutic alternatives.

Combining aztreonam with avibactam is the first approved in the European Union to restore the activity of aztreonam against MBL-producing and other β -lactamase bacteria. It provides a well-tolerated and effective treatment option against multidrug-resistant Gram-negative bacteria, including MBL-producing *Enterobacterales*, designated by WHO as a critical priority pathogen.

It should be noted that to date, there are still no effective beta-lactamase inhibitors active against Metallo- β -lactamase types NDM-1 (New Delhi MBL-1), VIM (Verona Integron-encoded MBL) and IMP (imipenem).

To sum up, new combinations are a promising tool in the fight against superinfection and limiting antibiotic resistance but are not the final solution to these problems. Further monitoring of possible resistance development mechanisms to combinations of cefepime/enmetazobactam and aztreonam/avibactam requires focused attention. Also, the search for new ways to overcome the decrease in sensitivity of multiresistant bacteria to existing antibiotics remains a significant challenge.

References:

1. Haytovych M.V. Individualization of antimicrobial therapy to minimise the development of resistance / M.V. Haytovych, O.A. Temirova, D.S. Polyakova // Ukrainian Medical Journal. – 2023. – 3 (155) – V/VI. – P. 5–7. – DOI: <https://doi.org/10.32471/umj.1680-3051.155.244011>
2. Internet resource
https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Addenda/Aztreonam-avibactam_addendum_22_May_2024.pdf
3. Rang & Dale's Pharmacology. – 9th edition. – ELSEVIER Churchill Livingstone, 2019. – 808 p
4. Internet resource
https://www.msmanuals.com/uk/professional/infectious-diseases/bacteria-and-antibacterial-medications/cephalosporins#%D0%9F%D0%BE%D0%BA%D0%B0%D0%B7%D0%B0%D0%BD%D0%BD%D1%8F_v13956832_uk
5. Internet resource
<https://www.msmanuals.com/uk/professional/infectious-diseases/bacteria-and-antibacterial-medications/monobactams>