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A.9 Ceftolozane/Tazobactam

MSF welcomes the application for the inclusion of ceftolozane/tazobactam in Section 6.2.3 “Reserve group antibiotics” in the WHO Model List of Essential Medicines (EML).

Ceftolozane belongs to the cephalosporin class of antimicrobials and tazobactam is a beta-lactamase inhibitor, added to inhibit the beta-lactamases produced by bacteria to destroy ceftolozane.

MSF would like to draw the attention of the Expert Committee on the following facts:

- Although ceftolozane/tazobactam is approved in Europe and USA for the treatment of complicated intra-abdominal infections and acute pyelonephritis, and complicated urinary tract infections among adults and children, and for hospital acquired pneumonia (including ventilator associated) among adults, and although it is active against extended-spectrum β -lactamase (ESBL) producing/ceftriaxone-resistant Enterobacterales, it is best reserved to be used exclusively as a last option for the treatment of difficult-to-treat resistant (DTR) *Pseudomonas aeruginosa* (*P.aeruginosa*) (carbapenem-resistant/MDR/XDR), whose prevalence is increasing in many settings including some where MSF is present (e.g. Middle East countries), and for which it does have advantages over the commonest available alternative, the polymyxins. To reserve ceftolozane + tazobactam exclusively as a last option for the treatment of DTR-*P.aeruginosa* (carbapenem-resistant/MDR/XDR) is in line with recent USA guidelines of the Infectious Diseases Society of America (IDSA 2022)¹, which recommends its use solely for DTR-*P.aeruginosa*, for which it is a 1st line choice, and recent European guidelines of the European Society of Clinical Microbiology and Infectious Diseases (ESCMIDD 2022)², in which there is explicit recommendation to avoid use for ESBL/ceftriaxone-R Enterobacterales for which there are other treatment options, again reserving it for DTR-*P.aeruginosa* as the sole first line option.

¹ Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America **2022**; Version 1.1. Available at <https://www.idsociety.org/practice-guideline/amr-guidance/>

² Paul M, Carrara E, Retamar P, Tängdén T, Bitterman R, Bonomo RA, de Waele J, Daikos GL, Akova M, Harbarth S, Pulcini C, Garnacho-Montero J, Seme K, Tumbarello M, Lindemann PC, Gandra S, Yu Y, Bassetti M, Mouton JW, Tacconelli E, Rodríguez-Baño J. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine). Clin Microbiol Infect. 2022 Apr;28(4):521-547.

- Currently, access is impossible in most resource limited settings due to prohibitive prices and lack of registration, barriers which should be worked on to guarantee that all patients in need can benefit (together with microbiology laboratory support for diagnosis). MSF emphasized that actions to foster access are sorely needed given very high prices and limited number of countries where ceftolozane/tazobactam is registered.
- The inclusion of ceftolozane/tazobactam in the EML will serve as a basis for National Essential Medicines lists and therefore will motivate additional manufacturers, particularly in low- and middle-income countries.

In light of this elements, MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to consider the inclusion of ceftolozane/tazobactam in the WHO Model List of Essential Medicines if it is included in the WHO Model List of Essential Medicines as a Reserve antibiotic (Section 6.2.3 Reserve group antibiotics) indicated only for the treatment of DTR-*P.aeruginosa*. MSF does not support ceftolozane/tazobactam for treatment of ESBL/ceftriaxone-R Enterobacterales or for treatment of *P.aeruginosa* still susceptible to other beta lactams or fluoroquinolones.



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