SHIONOGI

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Dear EML Secretariat,

Shionogi & Co., Ltd. hereafter called Shionogi) developed flomoxef sodium and obtained regulatory approval in Japan in 1988. Flomoxef sodium is currently approved in Japan, China, Taiwan and South Korea, where it is expected to be a potential treatment option of extended-spectrum β-lactamase-producing Enterobacterales (ESBL-PE).

Shionogi supports the inclusion of flomoxef sodium in the WHO Model Lists of Essential Medicines (EML) and Essential Medicines for Children (EMLc) for the indication of empiric treatment of community-acquired mild/moderate intra-abdominal infections (IAI) (e.g., appendicitis, cholecystitis, diverticulitis) and mild/moderate upper urinary tract infections (UTI) (e.g., pyelonephritis), in adults and children at high risk of infection caused by ESBL.

Flomoxef sodium is an oxacephem antibiotic belonging to the oxacephems subclass of second-generation cephalosporins that are not inactivated by ESBLs and narrow spectrum of β-lactamases enzymes. If included, it will be the first 2nd generation cephalosporin with activity against ESBL-PE in the EML. It has a good safety profile, and has been developed for use in neonates, children and adults.

ESBL enzymes confer resistance to most β-lactam antibiotics, including 3rd-generation cephalosporins and monobactams. Among them, ESBL class A enzymes (mainly CTX-M enzyme) are transmitted and disseminated easily and can confer resistance to other antibiotics like quinolones. ESBL-PE can cause community-acquired bacterial infections, such as UTI, IAI, and bloodstream infections, that if not appropriately and timely treated, can progress to sepsis and death. The main agents that are used to treat severe infections caused by ESBL-PE include piperacillin-tazobactam and meropenem, but there is no alternative recommendation for mild to moderate community-acquired intrabdominal infections and mild to moderate upper urinary tract infections.

In this context of high prevalence of community-acquired bacterial infections caused by ESBL-PE, poor diagnostic, stewardship and lack of recommended alternatives, carbapenems are used empirically for the treatment of non-severe infections causing increasing levels of carbapenem resistance. Flomoxef sodium is an ideal candidate to help address this urgent problem.

The inclusion of flomoxef sodium in WHO EML and EMLc would be important in the fight against AMR, will strengthen the strategy of repurposing old antibiotics as a tool to support antibiotic stewardship efforts at local, National and global levels, and will contribute to addressing antimicrobial resistance. Therefore, Shionogi recommends that the 24th Expert Committee on the selection and Use of Essential Medicines should include flomoxef sodium in the WHO EML and EMLc.

For Shionogi & Co., Ltd.

Yosuke Miharu
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