KEMRI | Wellcome Trust

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31st March 2023

Dear EML Secretariat,

RE: Application from GARDP for inclusion of flomoxef sodium in the WHO Model Lists of Essential Medicines (EML) and Essential Medicines for Children (EMLc).

I am a Kenyan doctor specialising in research and care for neonatal sepsis and Public Health writing to support the inclusion of flomoxef sodium in the EML. My context is of increasing resistance and a severely limited selection of affordable and appropriate antibiotics available. I am involved in the preparation and conduct of a large international clinical trial, NeoSep1 (ISRCTN48721236), evaluating new combinations of generic antibiotics, including flomoxef sodium and comparing them to currently used antibiotic regimens including WHO-recommended empiric antibiotics for neonatal sepsis.

Antimicrobial resistance (AMR) poses a significant threat to child survival globally, especially in resource-limited settings where its burden is highest. Extended spectrum β-lactamase-producing Enterobacterales (ESBL-PE) significantly contribute to AMR, globally. ESBL-PE carriage and acquisition is common among neonates admitted to our hospital in Kilifi,[1] and comprise about one-third of Gram-negative clinical isolates cultured from hospitalised children under the age of five years.[2] Preliminary results (unpublished) of an ongoing blood culture and environmental surveillance in three Level 4 county hospitals in Kenya show overall ~80% and ~35% resistance to ampicillin and gentamicin respectively, and an ESBL-PE prevalence ranging between 35% and 90% across the three sites. Limited availability of diagnostic tools to guide therapeutic decisions means that clinicians are often using ineffective regimens such as ampicillin plus gentamicin or turning to carbapenems to treat community and hospital acquired infections where other agents might save the use of these. Alternative regimens active against ESBL-PE are therefore urgently needed to effectively treat infections and improve child survival, while preserving other 'last-line' antibiotics.

Flomoxef sodium has a long history of safe use for the empiric treatment of sepsis in children and neonates. Flomoxef has *in vitro* activity against ESBL-PE and is a potential carbapenem-sparing option in the face of rising AMR. Inclusion of flomoxef sodium in WHO EML would facilitate adoption by National EML and updating of treatment guidelines in low- and middle countries, assuring availability and accessibility to vulnerable patients at most need, given that it is an off-patent antibiotic. Therefore, I strongly recommend that the Expert Committee on Selection and Use of Essential

Medicines considers this important product, that addresses a public health need, for the WHO EML and the EMLc.

Yours sincerely,

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References

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2. Williams PCM, Waichungo J, Gordon NC, et al. The potential of fosfomycin for multi-drug resistant sepsis: an analysis of in vitro activity against invasive paediatric Gram-negative bacteria. *Journal of medical microbiology* 2019;68(5):711-19. doi: 10.1099/jmm.0.000973 [published Online First: 2019/04/18]