CORRESPONDENCE

Treatment Options for Carbapenem-Resistant Gram-Negative Infections

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in issue 20–21/2018

Oral Fosfomycin—Supplemental Information Necessary

This review gives general therapy recommendations, including for oral fosfomycin, for which it lists heart failure as one of the dangerous adverse reactions of the active substance (1). As they stand, these points are ambiguous, to say the least, and require clarification. *Table 1* of the review lists oral fosfomycin. However, the oral delivery form of the substance is only approved for the treatment of uncomplicated urinary tract infections (2). Infection by 3/4 multiresistant Gram-negative (MRGN) pathogens are not considered to be straightforward, and oral fosfomycin is inappropriate for treating systemic infections due to its poor absorption and its resulting low levels in tissues. In contrast, intravenous fosfomycin achieves high therapeutic levels and, according to the current S2k guideline of the Paul Ehrlich Society for Chemotherapy, represents an important therapeutic option in the combination therapy of 3/4 MRGN, especially in intensive care (3). However, it is not listed by the authors in the treatment recommendations given in *Table 2*. Thus, a relevant therapy option remains hidden. Listing heart failure in the text as a dangerous adverse event of the drug is also misleading. Heart failure as a direct adverse event of fosfomycin is not documented either in the summary of product characteristics or in current reviews on drug safety (4). In summary, the authors unfortunately

did not adequately differentiate between the different areas of use for oral and intravenous administration of fosfomycin. Only intravenous fosfomycin should be listed as a treatment option for 3/4 MRGN infections. DOI: 10.3238/arztebl.2019.0115a

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Conflict of interest statement

The author has been reimbursed for conference fees and travel expenses, and has received speaking honoraria, from Basilea, Correvio, Accelerate, Infecto-Pharm, Pfizer, MSD, and Abbott.

In Reply:

We are grateful for the correspondence and are of course happy to address controversial or unclear issues.

We are likewise convinced that intravenous fosfomycin is an important antibiotic against 3/4 MRGN pathogens, and we use it regularly. For this reason, we listed it several times in *Table 1*, *Table 2*, in the article text, and in the Key Messages. *Table 2*—as stated in the N.B.—is to be considered as a series of therapy proposals (1). It makes sense to decide which antibiotic scheme should be used based on interdisciplinary discussions about patient- and pathogen-specifics for individual cases.

Therapy recommendations initially refer to carbapenem-resistant pathogens without a description of the severity of infection. From these options (and possibly others, based on specific considerations of the patient with reference especially to the infection focus and relevant contraindications), a therapy concept can be selected individually, whereby a patient with sepsis should generally receive intravenous treatment.

In *Table 1*, we explicitly referred to uncomplicated lower urinary tract infections for oral fosfomycin. We have authorized a correction of the article to clarify that oral fosfomycin is generally only approved for uncomplicated lower urinary tract infections. Whether or not oral fosfomycin is an option in complicated

urinary tract infections should be tested in RCTs. However, if it is the only antibiotic with susceptibility, we certainly see it as an option to be discussed—provided that no better alternatives are available.

We agree that electrolyte control normally works in ICU patients, and heart failure is a rare adverse reaction, with a probability of 0.07% (2). Nevertheless, we would like to draw attention to electrolyte imbalance as an important adverse reaction, so that it is not overlooked. DOI: 10.3238/arztebl.2019.0115b

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Conflict of interest statement

The author declares that no conflict of interest exists.