**Abstract**

Background: FO43* (fosfomycin, FOS) is a new-generation oral antibiotic that exhibits unbalanced activity against Gram-negative (GN) and positive (GP) organisms, in contrast with previous classes. The GN strains are known to present an unbalanced MIC endpoint, which could limit the clinical development in the USA for the treatment of uncomplicated urinary tract infections (UTIs). A new formulation every 6 hours (50 mg/L) is being evaluated for this therapeutic purpose. An online formulation (FO43* consortium) test was performed in 230 clinical isolates, including 146/230 (63.5%) of Enterobacteriaceae (EB) and 86/230 (36.5%) of GP organisms. The objective of this study was to determine the MIC susceptibility and potential mechanisms of resistance for FO43* using agar dilution (AD) and broth microdilution (BMD) methods.

Methods: A total of 234 GN and GP isolates from USA medical centers during 2016 were included. FO43* (25 µg/mL) and clindamycin (2 µg/mL) resistance were determined by disk diffusion. MICs were determined by FO43* (BMD) and clindamycin (susceptibility test) by AD. The MIC was defined as the lowest concentration yielding no visible growth. MIC results were compared by AD and BMD methods using the CLSI breakpoint criteria. Correlation of MIC values with broth microdilution (BMD) was generally one to two dilutions €30 lower than AD. Only 4/234 (1.7%) of FO43* isolates were categorized susceptible by disk and MIC. There were no major or minor errors.

Results: A total of 354 isolates from USA medical centers during 2016 were included. FO43* (25 µg/mL) and clindamycin (2 µg/mL) resistance were determined by disk diffusion. MICs were determined by FO43* (BMD) and clindamycin (susceptibility test) by AD. The MIC was defined as the lowest concentration yielding no visible growth. MIC results were compared by AD and BMD methods using the CLSI breakpoint criteria. Correlation of MIC values with broth microdilution (BMD) was generally one to two dilutions €30 lower than AD. Only 4/234 (1.7%) of FO43* isolates were categorized susceptible by disk and MIC. There were no major or minor errors.

Conclusion: FO43* (25 µg/mL) is an active agent that exhibits unbalanced activity against Gram-negative (GN) and positive (GP) organisms, in contrast with previous classes. FO43* is an unbalanced MIC endpoint, which could limit the clinical development in the USA for the treatment of uncomplicated UTIs. A new formulation every 6 hours (50 mg/L) is being evaluated for this therapeutic purpose. An online formulation (FO43* consortium) test was performed in 230 clinical isolates, including 146/230 (63.5%) of Enterobacteriaceae (EB) and 86/230 (36.5%) of GP organisms. The objectives of this study were to determine the MIC susceptibility and potential mechanisms of resistance for FO43* using agar dilution (AD) and broth microdilution (BMD) methods.