Carbapenems are a widely used subclass of antibiotics belonging to the beta-lactams family, because they have been observed to be safe and effective in the treatment of multidrug-resistant Gram-negative bacterial infections. But today they are only available in hospital settings as intravenous therapeutics for such indications. Tebipenem (TBP) is the first oral carbapenem for the treatment of complicated urinary tract infection (cUTI) and acute pyelonephritis to help patients to avoid hospitalizations and/or transition patients home after IV therapy. Tebipenem has been shown to be active in vitro against prevalent UTI Enterobacterales species, including those producing ESBLs and/or AmpC enzymes (derepressed chromosomal or plasmid-acquired).

In this study, the performance of ETEST ® TBP (not yet available on the market), an in vitro technique for determining the MICs of Tebipenem for Enterobacterales, was established against broth microdilution (BMD) CLSI reference method for a large panel of isolates.

### MATERIAL AND METHOD

#### Bacterial strains

A set of 67 Enterobacterales strains comprising 42 E. coli, 15 K. pneumoniae and 10 E. cloacae (including extended spectrum beta-lactamase- and carbapenemase-producers Enterobacterales) were tested by ETEST® TBP and BMD.

QC organisms tested were Escherichia coli ATCC® 25922™, Staphylococcus aureus ATCC® 29213™, P. aeruginosa ATCC® 27853™, and Enterococcus faecalis ATCC® 29212™ following CLSI QC guidelines.

#### Method

The isolates were sub-cultured on Columbia agar plates supplemented with 5% sheep blood before testing. After incubation, suspensions of the isolates were prepared in 0.85% saline. These suspensions were used to inoculate both BMD (with 1/100 dilution) and ETEST® TBP plates.

Results were read after 16-20 hours of incubation at 35°C+/−2°C in ambient air for both methods.

Results were analyzed using the provisional breakpoints for Tebipenem (S ≤ 0.125 µg/mL, I=0.25 µg/ml, R ≥ 0.5 µg/mL). Performance was evaluated using FDA performance criteria, essential agreement (EA, ≥ 90%), category agreement (CA, ≥ 90%), major error rate (ME, ≤3.0%) and very major error rate (VME, ≤2.0%).

### RESULTS

All the QC strains were within the CLSI ranges.

For the panel results, see table 1 : Performance for ETEST® TBP on each species.

### CONCLUSION

This first and preliminary study shows that the new ETEST® TBP is found to be substantially equivalent to the CLSI reference method. ETEST® TBP could be a valuable tool for determining Tebipenem MIC for Enterobacterales harboring various resistance mechanisms. ETEST® TBP needs clinical studies in order to be IVD cleared (FDA).

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