Tebipenem In vitro Activity against a Collection of Pathogens Responsible for Urinary Tract Infections in the US

R.E. Mendes\(^a\), I.A. Critchley\(^b\), N. Cotonero\(^c\), J.M. Streit\(^d\), H.S. Sader\(^e\), M. Castanheira\(^f\)

\(^a\)JMI Laboratories, North Liberty, IA, USA, \(^b\)Spero Therapeutics, Cambridge, MA, USA

**Introduction**

- Enterobacteriaceae—especially Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis—are widely implicated in urinary tract infection (UTI).
- Many oral agents are used to manage UTIs, but their clinical usefulness has been compromised by the increased prevalence of extended-spectrum β-lactamases (ESBL) and carbapenemases.

**Materials and Methods**

**Bacterial organisms**

- A total of 5,776 Enterobacteriaceae collected from 52 medical centers in 9 US Census Divisions were recovered from urine samples during the 2010–2012 STEWARDS Surveillance Program and included in the study.
- Bacterial identification was confirmed by standard algorithms supported by matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany).

**Susceptibility testing**

- Isolates were tested for susceptibility by broth microdilution following the Clinical and Laboratory Standards Institute (CLSI) M06 (2016) guidelines.
- Fractional inhibitory concentration (FIC) indices were calculated for tebipenem and comparator agents based on predefined breakpoints provided by the National Committee for Clinical Laboratory Standards (CLSI). M07 (2016).

**Results**

- E. coli comprised 65.4% of all Enterobacteriaceae pathogen isolates included in the study and associated with UTI, followed by K. pneumoniae (14.3%) and P. mirabilis (6.6%) (Table 1).
- Other pathogens comprised 25 species or species groups (13.7%).
- In general, E. coli, K. pneumoniae, and P. mirabilis were non-susceptible to tebipenem with FIC indices of ≥0.5 (Table 1).
- E. coli isolates were susceptible to tebipenem (FIC >0.5) compared to K. pneumoniae, whereas non-susceptibility rates for amoxicillin-clavulanate and cefazolin were not observed (Table 1).
- Other oral cephalosporins (e.g., cefazolin and ceftriaxone) showed susceptibility rates >90% (Table 2).
- Other pathogens comprised 25 species or species groups (13.7%).

**Conclusions**

- Tebipenem displayed potent activity against Enterobacteriaceae pathogens causing UTI among patients in the US. The in vivo potency of oral tebipenem was similar to that of the intravenous parenteral.
- In general, these data showed compromised activity of oral agents used for treating UTI. These data support the development of tebipenem as an oral option for management of UTI in the US.

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**References**


**Contact**

R.E. Mendes
JMI Laboratories
185 North Liberty Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3371
Fax: (319) 665-3371
Email: rsmendes@jmilib.com

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**Table 1. Antimicrobial activity of tebipenem and comparator agents tested against the main organisms and organism groups**

<table>
<thead>
<tr>
<th>Organism/organism group (no. of isolates)</th>
<th>MIC range (µg/mL)</th>
<th>Tebipenem</th>
<th>Cefazolin</th>
<th>Aztreonam</th>
<th>Ceftazidime</th>
<th>Ceftriaxone</th>
<th>Meropenem</th>
<th>Imipenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td></td>
<td>0.03 ≤0.12</td>
<td>16 ≤128</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;32</td>
<td>≤0.12 ≤0.12</td>
<td>≤0.12 ≤0.12</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td>0.03 ≤0.12</td>
<td>16 ≤128</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;32</td>
<td>≤0.12 ≤0.12</td>
<td>≤0.12 ≤0.12</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td></td>
<td>0.03 ≤0.12</td>
<td>16 ≤128</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;16</td>
<td>&gt;16 &gt;32</td>
<td>≤0.12 ≤0.12</td>
<td>≤0.12 ≤0.12</td>
</tr>
</tbody>
</table>

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**Table 2. Antimicrobial activity of tebipenem and comparator agents tested against Enterobacteriaceae and other pathogens**

- Ertapenem, imipenem, nitrofurantoin, and piperacillin-tazobactam were also active against most Enterobacteriaceae and other pathogens tested.
- MIC results of ≥2 µg/mL for ceftazidime, aztreonam, and/or ceftriaxone were analyzed separately, and presumptively for the presence of ESBL (Table 2).
- Other pathogens comprised 25 species or species groups (13.7%).

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**Figure 1. Rates of non-susceptibility for amoxicillin-clavulanate, cefazolin (predicts nonsusceptibility to oral cephalosporins), levofloxacin, and trimethoprim-sulfamethoxazole (TMP-SMA) against E. coli (Figure 1A), K. pneumoniae (Figure 1B), and P. mirabilis (Figure 1C).** Criteria as published by CLSI (2021).