Breakpoints for temocillin

Addendum (April 2020) to EUCAST breakpoint tables v. 10.0

Breakpoints to be included in EUCAST breakpoint tables v 11.0, January 2021

Temocillin is a beta-lactam agent based on a penam core and a derivative of ticarcillin. The 6-methoxy and the other side chains confer an unusual spectrum for a penam, including relative resistance to a range of beta-lactamases and no useful activity against gram-positive microorganisms, most non-fermentative gram-negative bacteria and most of the common anaerobic pathogens.

Temocillin is licensed for use in Belgium, the United Kingdom, France and Germany.

Antimicrobial susceptibility testing methodology

**Broth microdilution**
- Broth microdilution according to ISO 20776-1 for non-fastidious organisms in un-supplemented Mueller-Hinton broth.

**Disk diffusion**
- Disk diffusion according to EUCAST methodology for non-fastidious organisms on un-supplemented Mueller-Hinton agar. Ignore isolated colonies within the inhibition zone when reading temocillin 30 µg inhibition zones (reading examples below).

Enterobacterales breakpoints are valid only for *E. coli*, *Klebsiella* spp. (except *K. aerogenes*), *P. mirabilis*:
- \( S \leq 0.001, R > 16 \text{ mg/L} \)

The R breakpoint is the same as the ECOFF for most target species. The wild-type population has been placed in the I group to emphasise the need for high exposure to cover the entire wild-type (1 – 16 mg/L) of relevant species.

**Clinical breakpoints for temocillin** have (following general consultation 2019) been set by EUCAST as follows:

<table>
<thead>
<tr>
<th>Organisms</th>
<th>MIC breakpoint (mg/L)</th>
<th>Disk content (µg)</th>
<th>Zone diameter breakpoint (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( S \leq )</td>
<td>( R &gt; )</td>
<td>( S \geq )</td>
</tr>
<tr>
<td>Enterobacterales (<em>E. coli</em>, <em>Klebsiella</em> spp. (except <em>K. aerogenes</em>), <em>P. mirabilis</em> only)</td>
<td>0.001</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>PK/PD (non-species related) breakpoints</td>
<td>IE</td>
<td>IE</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^1\) Ignore isolated colonies within the inhibition zone.

**Qualifiers**

| Clinical qualifications | Species-related breakpoints apply to isolates from patients with complicated and more severe urinary tract infections including urosepsis, but excluding severe sepsis and septic shock. There are insufficient data to recommend breakpoints and dosing regimens for pneumonia or other invasive infections |
Dosage

Breakpoints apply to high-exposure dosing regimen of 2 g x 3 iv

Additional comment

Data from mouse non-severe pyelonephritis model supports a breakpoint of R > 16 mg/L, but only with a dosing regimen of 2 g x 3. An "R" breakpoint below 16 mg/L (for example 8 mg/L, which has been used by some countries) would split the wild type of the relevant species believed to be good targets for temocillin. Using a target %T>MIC of 35%, satisfactory target attainment rates can only be achieved in systemic infections using doses of 2 g every 8 hours, i.e. doses above those currently licensed. High urinary concentrations may permit the use of lower-exposure dosing regimens such as 2 g every 12 hours for lower urinary tract infections complicated by comorbidities or caused by species resistant to other drug classes.

Reference. Temocillin Rationale Document v1.0 (http://www.eucast.org/documents/rd/)

Quality control ranges for MIC and disk diffusion tests on temocillin are as follows:

<table>
<thead>
<tr>
<th>Organisms</th>
<th>MIC (mg/L)</th>
<th>Disk content (µg)</th>
<th>Inhibition zone diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Target</td>
<td>Range</td>
<td>Target</td>
</tr>
<tr>
<td>E. coli ATCC 25922</td>
<td>16</td>
<td>8-32</td>
<td>30</td>
</tr>
</tbody>
</table>

¹ Ignore isolated colonies within the inhibition zone (see examples below).

MIC/zone diameter correlates for temocillin

**Temocillin 30 µg disk vs. MIC**

*E. coli, K. pneumoniae and P. mirabilis*

![MIC/zone diameter correlates for temocillin](chart.png)
Examples of reading temocillin inhibition zones

Ignore isolated colonies within the inhibition zone.