Streptococcus agalactiae

Calibration of zone diameter breakpoints to MIC values

Version 4.0
January 2020
Streptococcus agalactiae
MIC and zone diameter correlates

• The following histograms present inhibition zone diameter distributions from EUCAST antimicrobial susceptibility testing. In most, the different colours of the bars indicate different MIC values. In some, the colours of the bars indicate a resistance gene or a resistance mechanism.

• The distributions include data for wild-type isolates and for isolates with acquired resistance mechanisms. A large number of isolates with MIC values close to the edge of the wild-type distribution and/or close to EUCAST clinical breakpoints were intentionally included. These distributions can not be used to infer resistance rates or the performance of the tests with routine isolates.

• For some agents, isolates were tested on more than one occasion, including parallel tests with disks and media from several manufacturers. When this is the case, data are presented as both the “number of isolates tested” and the “total number of MIC-zone diameter correlates”, including replicate tests and parallel tests with disks and media from different sources.
Streptococcus agalactiae
Materials and methods

• Antimicrobial susceptibility testing was performed on clinical isolates of *Streptococcus agalactiae*, including isolates with known resistance mechanisms. Disk diffusion was performed on MH-F media according to EUCAST methodology and MIC determination was performed with the ISO broth microdilution method using MH-F broth.

• The distributions of MIC vs. zone diameter in this presentation are the result of a collaboration between EUCAST, JMI Laboratories (USA) and Laboratory Specialists Inc. (USA).

• This presentation is based on EUCAST Clinical Breakpoint Tables v. 10.0.
# Changes from previous version (3.0)

## Changes

<table>
<thead>
<tr>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MIC and zone diameter breakpoints changed for levofloxacin, minocycline and linezolid.</td>
</tr>
<tr>
<td>• Data added for linezolid.</td>
</tr>
<tr>
<td>• New distribution for tedizolid.</td>
</tr>
</tbody>
</table>
**Explanation of graphs:**

- These graphs show zone diameter distributions with MIC values or resistance mechanisms as coloured bars. Colours are related to current EUCAST MIC breakpoints.

**Agent X**

- Zone diameter breakpoint

**MIC (mg/L)**
- ≥8
- 4
- 2
- 1
- 0.5
- 0.25

- No of observations

**Inhibition zone diameter (mm)**

**Agent Y**

**MIC (mg/L)**
- ≥64
- 32
- 16
- 8
- 4
- 2
- 1
- 0.5
- ≤0.25

- No of observations

**Inhibition zone diameter (mm)**
Benzylpenicillin 1 unit vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

**Breakpoints**
- **MIC**
  - \( S \leq 0.25, \ R > 0.25 \text{ mg/L} \)
  - ECOFF: 0.125 mg/L
- **Zone diameter**
  - \( S \geq 18, \ R < 18 \text{ mm} \)
Levofloxacin 5 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

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**Breakpoints**

<table>
<thead>
<tr>
<th>MIC</th>
<th>S≤0.001, R&gt;2 mg/L</th>
<th>ECOFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S≥50, R&lt;17 mm</td>
<td>2 mg/L</td>
</tr>
</tbody>
</table>
Moxifloxacin 5 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

**Breakpoints**

<table>
<thead>
<tr>
<th>MIC</th>
<th>S≤0.5, R&gt;0.5 mg/L</th>
<th>ECOFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S≥19, R&lt;19 mm</td>
<td>0.5 mg/L</td>
</tr>
</tbody>
</table>

**MIC** (mg/L)
- 4
- 2
- 1
- 0.5
- 0.25
- 0.125
- 0.06
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance.

Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and as “susceptible increased exposure” (I) to levofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.

**Breakpoints**
- **Levofoxacin MIC**  
  - S≤0.001, R>2 mg/L
- **Norfloxacin zone diameter (screen)**  
  - S≥12 mm

**ECOFF**
- 2 mg/L
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance.

Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and as “susceptible increased exposure” (I) to levofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.

Breakpoints
Moxifloxacin MIC $S \leq 0.5$, $R > 0.5$ mg/L
Norfloxacin zone diameter (screen) $S \geq 12$ mm

ECOFF 0.5 mg/L
Vancomycin 5 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

### Breakpoints

<table>
<thead>
<tr>
<th>MIC</th>
<th>Zone diameter</th>
<th>ECOFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>S ≤ 2, R &gt; 2 mg/L</td>
<td>S ≥ 13, R &lt; 13 mm</td>
<td>1 mg/L</td>
</tr>
</tbody>
</table>
Erythromycin 15 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

### Breakpoints

<table>
<thead>
<tr>
<th>MIC</th>
<th>S≤0.25, R&gt;0.5 mg/L</th>
<th>ECOFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S≥21, R&lt;18 mm</td>
<td>0.25 mg/L</td>
</tr>
</tbody>
</table>

### MIC (mg/L)

- ≥16
- 8
- 4
- 2
- 1
- 0.5
- 0.25
- 0.125
- 0.06
- 0.03
- 0.016
Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.
Erythromycin 15 µg vs. Clarithromycin MIC
*S. agalactiae*, 32 isolates

(1 data source)

Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.

**Breakpoints**

- **Clarithromycin MIC**
  - S ≤ 0.25, R > 0.5 mg/L
- **Erythromycin zone diameter**
  - S ≥ 21, R < 18 mm
Erythromycin 15 µg vs. Roxithromycin MIC
*S. agalactiae*, 32 isolates

(1 data source)

Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.

Breakpoints
Roxithromycin MIC  
S≤0.5, R>1 mg/L

Erythromycin zone diameter  
S≥21, R<18 mm
Telithromycin 15 µg vs. MIC
*S. agalactiae*, 32 isolates

1 data source

**Breakpoints**
- **MIC**
  - S ≤ 0.25, R > 0.5 mg/L
- **Zone diameter**
  - S ≥ 20, R < 17 mm
Clindamycin 2 µg vs. MIC
S. agalactiae, 32 isolates

(1 data source)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>0.5</td>
<td>6</td>
</tr>
<tr>
<td>0.25</td>
<td>5</td>
</tr>
<tr>
<td>0.125</td>
<td>4</td>
</tr>
<tr>
<td>0.06</td>
<td>3</td>
</tr>
<tr>
<td>0.03</td>
<td>2</td>
</tr>
<tr>
<td>0.016</td>
<td>1</td>
</tr>
</tbody>
</table>

Breakpoints
- MIC: S≤0.5, R>0.5 mg/L
- Zone diameter: S≥17, R<17 mm

ECOFF: 0.5 mg/L
Minocycline 30 µg vs. MIC
S. agalactiae, 32 isolates

(1 data source)

No of observations

Inhibition zone diameter (mm)

Breakpoints
MIC
S≤0.5, R>0.5 mg/L

Zone diameter
S≥23, R<23 mm

ECOFF
0.5 mg/L

MIC (mg/L)
- ≥32
- 16
- 8
- 4
- 2
- 1
- 0.5
- 0.25
- 0.125
- 0.06
Tetracycline 30 µg vs. MIC
S. agalactiae, 32 isolates
(1 data source)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Breakpoints</th>
<th>ECOFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥32</td>
<td>S≤1, R&gt;2 mg/L</td>
<td>1 mg/L</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.125</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No of observations

Inhibition zone diameter (mm)
Isolates susceptible to tetracycline are also susceptible to doxycycline and minocycline, but some resistant to tetracycline may be susceptible to minocycline and/or doxycycline. An MIC method should be used to test doxycycline susceptibility of tetracycline resistant isolates if required.

**Breakpoints**

- **Doxycycline MIC**
  - S≤1, R>2 mg/L

- **Tetracycline zone diameter**
  - S≥23, R<20 mm

(1 data source)
Tetracycline 30 µg vs. Minocycline MIC
*S. agalactiae*, 32 isolates

(1 data source)

Isolates susceptible to tetracycline are also susceptible to doxycycline and minocycline, but some resistant to tetracycline may be susceptible to minocycline and/or doxycycline. An MIC method should be used to test doxycycline susceptibility of tetracycline resistant isolates if required.

**Breakpoints**
- Minocycline MIC
  - S≤0.5, R>0.5 mg/L
- Tetracycline zone diameter
  - S≥23, R<20 mm

**ECOFF**
0.5 mg/L
Tigecycline 15 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

**Breakpoints**

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>S ≤ 0.125, R &gt; 0.125 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S ≥ 19, R &lt; 19 mm</td>
</tr>
</tbody>
</table>
Linezolid 10 µg vs. MIC
*S. agalactiae*, 79 isolates (186 correlates)

(4 data sources)

**Breakpoints**
- MIC: S≤2, R>2 mg/L
- Zone diameter: S≥19, R<19 mm

**ECOFF**: 2 mg/L
Tedizolid 2 µg vs. MIC
S. agalactiae, 40 isolates (300 correlates)

(2 data sources)

No of observations

MIC (mg/L)
- 0.5
- 0.25
- 0.125

Inhibition zone diameter (mm)

Breakpoints
- MIC: S≤0.5, R>0.5 mg/L
- Zone diameter: S≥18, R<18 mm
Chloramphenicol 30 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>0.5</td>
<td>0</td>
</tr>
</tbody>
</table>

Inhibition zone diameter (mm)

Breakpoints
- MIC: S≤8, R>8 mg/L
- Zone diameter: S≥19, R<19 mm
Rifampicin 5 µg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

**Breakpoints**

- **MIC**
  - S ≤ 0.06, R > 0.5 mg/L
- **Zone diameter**
  - S ≥ 21, R < 15 mm
Trimethoprim-sulfamethoxazole 1.25-23.75 μg vs. MIC
*S. agalactiae*, 32 isolates

(1 data source)

Breakpoints

**MIC**
S≤1, R>2 mg/L

**Zone diameter**
S≥18, R<15 mm