<table>
<thead>
<tr>
<th>Rule No</th>
<th>Organisms</th>
<th>Indicator Agent*</th>
<th>Agents affected*</th>
<th>Rule</th>
<th>Remarks</th>
<th>Grade</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-Lactams</strong></td>
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</tbody>
</table>
| 1 | *E. coli, P. mirabilis* | ampicillin | piperacillin | IF resistant to ampicillin, THEN report resistant to piperacillin regardless of test result  
IF susceptible to ampicillin, THEN report as susceptible to piperacillin | | A | Drusano, Schimpff, & Hewitt, 1984 |
<p>| 3 | <em>Enterobacter</em> spp., <em>K. aerogenes</em>, <em>Citrobacter freundii</em> complex, <em>Hafnia alvei</em> | cefotaxime, ceftiraxone, ceftazidime | cefotaxime, ceftiraxone, ceftazidime | IF susceptible in vitro to cefotaxime, ceftiraxone or ceftazidime, THEN EITHER add a note that monotherapy with cefotaxime, ceftiraxone or ceftazidime as well as combination therapy of these agents with an aminoglycoside should be discouraged owing to risk of selecting resistance, OR suppress the susceptibility testing results for these agents | Selection of AmpC de-repressed cephalosporin-resistant mutants may occur during therapy. The risk is relatively high in <em>Enterobacter</em>, <em>K. aerogenes</em> and <em>Citrobacter</em> and low in <em>Morganella</em> and <em>Serratia</em>. For <em>Hafnia alvei</em> in-vitro mutation rates are similar to <em>Enterobacter</em> or <em>Citrobacter</em>. The use of a 3rd generation cephalosporin in combination with an aminoglycoside may also lead to failure by selection of resistant mutants. he combination with a quinolone, however, has found to be protective, although the clinical utility of this combination is not known. The selection risk is absent or much diminished for cefepime | A | Sanders &amp; Sanders, 1988; Choi et al., 2008; Harris &amp; Ferguson, 2012; Kohlmann, Bahr, &amp; Gatermann, 2018 |</p>
<table>
<thead>
<tr>
<th></th>
<th>Enterobacterales</th>
<th>Antibiotics</th>
<th>Susceptibility Notes</th>
<th>A</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Serratia spp., Morganella morganii, Providencia spp</td>
<td>cefotaxime, ceftriaxone, ceftazidime</td>
<td>IF susceptible to cefotaxime, ceftriaxone or ceftazidime, THEN note that monotherapy with cefotaxime, ceftriaxone or ceftazidime may infrequently select resistant mutants</td>
<td>A</td>
<td>Sanders &amp; Sanders, 1988; Choi et al., 2008; Harris &amp; Ferguson, 2012; Kohlmann, Bähr, &amp; Gatenmann, 2018</td>
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<tr>
<td>5</td>
<td>Enterobacter spp., K. aerogenes, Citrobacter freundii, Serratia spp, Morganella morganii, Hafnia alvei</td>
<td>cefuroxime</td>
<td>IF susceptible to cefuroxime, THEN report cefuroxime and/or any other 2nd generation cephalosporin as resistant</td>
<td>C</td>
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<tr>
<td>6</td>
<td>E. coli, Klebsiella spp. (except K. aerogenes), Raoultella spp.</td>
<td>cefotaxime, ceftriaxone, ceftazidime, cefepime, piperacillin-tazobactam, amoxicillin-clavulanic acid</td>
<td>IF resistant to any 3rd generation (ceftaxime, ceftriaxone, ceftazidime) or 4th generation (cefepime) cephalosporin AND susceptible to piperacillin-tazobactam or amoxicillin-clavulanic acid, THEN report as tested. This phenotype is most often caused by ESBL production. ESBL producers sometimes test as susceptible to beta-lactam/beta-lactamase-inhibitor combinations. The use of these combinations in infections caused by ESBL-producers has historically been a matter of controversy. A number of studies have shown that they may be safe provided appropriate dosing is used. One publication indicates that carbapenem therapy may be superior to piperacillin-tazobactam, as measured by 30-day mortality and primarily in patients with terminal cancer</td>
<td>A</td>
<td>Retamar, López-Cerero, Muniaín, Pascual, &amp; Rodríguez-Baño, 2013; Rodríguez-Baño, Cisneros, Gudiol, &amp; Martínez, 2014; Ofer-Friedman et al., 2015; Tamma et al., 2015; Gutiérrez-Gutiérrez et al., 2016 Harris et al., 2018;</td>
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</tbody>
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### Enterobacterales

**7** E. coli, Klebsiella spp. (except K. aerogenes), Raoultella spp.

- cefotaxime, ceftriaxone, ceftazidime, cefepime
- cefotaxime, ceftriaxone, ceftazidime, cefepime

**Enterobacterales**

**8** Enterobacterales except Salmonella spp.

- ciprofloxacin
- all fluoroquinolones

**Fluoroquinolones**

**9** Serratia spp. Providencia spp. Morganella morganii

- tigecycline
- tigecycline

**Tetracyclines**

**10** Enterobacterales

- aminoglycosides
- aminoglycosides

**Aminoglycosides**

This phenotype is most often caused by ESBL production. Available evidence indicates that the cephalosporin phenotype predicts treatment outcome, although there is still a paucity of clinical data outside the urinary tract.

Fluoroquinolones

- IF resistant to ciprofloxacin,
  THEN report as resistant to all fluoroquinolones
- IF susceptible to ciprofloxacin,
  THEN report other fluoroquinolones as tested

- Acquisition of at least two target mutations in either gyrA or gyrB plus parC. The AAC(6')-Ib-cr enzyme partially inactivates ciprofloxacin but not levofloxacin; however, with current breakpoints this difference cannot be detected

Tetracyclines

- Tigecycline has poor activity against these species and should be reported as resistant irrespective of susceptibility testing result

- Data on efficacy of tigecycline towards these organisms is scarce

Aminoglycosides

- Breakpoints for aminoglycosides are being revised during 2019 after which all rules pertaining to aminoglycosides will be revisited.

*unless indicated, all names refer to agents without inhibitors
References


