

Rule No.	Organism(s)	Indicator Agent	Agent(s) Affected*	Rule	Remarks	Grade	References
<b>Beta-lactams</b>							
1	<i>Enterococcus faecalis</i> and <i>E. faecium</i>	ampicillin	amoxicillin, ureidopenicillins and imipenem	IF resistant to ampicillin, THEN report as resistant to ureidopenicillins and imipenem	<p>Alterations in PBP5 lead to reduced affinity for beta-lactams. Although ampicillin resistance predicts the test result for imipenem, this is not true for ampicillin susceptibility</p> <p>In <i>E. faecalis</i>, susceptibility to ampicillin, amoxicillin and piperacillin (with and without beta-lactamase inhibitor) can be inferred from ampicillin in 98% of isolates. In other <i>Enterococcus</i> spp. (including <i>E. faecium</i>), susceptibility to these agents is uncommon and isolates resistant to ampicillin should not be reported susceptible to either amoxicillin or piperacillin (with and without inhibitor)</p> <p>In <i>E. faecalis</i>, ampicillin susceptible isolates are generally susceptible also to amoxicillin (with and without clavulanic acid) and susceptible increased exposure to piperacillin (without or without tazobactam). However, since some of the isolates can be resistant to piperacillin despite being ampicillin susceptible, it is recommended to test the agent to be reported.</p>	C	Weinstein, et al., 2004. Hasegawa, et al. 2025
<b>Aminoglycosides</b>							
2	<i>Enterococcus</i> spp.	gentamicin	gentamicin, streptomycin	<p>IF high-level resistant to gentamicin, THEN report with a warning that combinations of this and other aminoglycosides, except for streptomycin (see below), are no longer synergistic AND test for streptomycin high-level resistance</p> <p>IF high-level resistance to gentamicin is not detected, THEN report gentamicin as effective for synergy purposes</p>	Enterococci with high-level resistance to gentamicin usually express the bifunctional aminoglycoside modifying enzyme AAC(6')-APH(2'') that inactivates many aminoglycosides except streptomycin. Animal models have shown decreased efficacy for combinations of beta-lactams and gentamicin in such strains	B	Moellering, et al., 1979; Daigle, et al., 1999

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3	<i>Enterococcus</i> spp.	streptomycin	streptomycin	IF high-level resistant to streptomycin, THEN report with a warning that combinations of this aminoglycoside with beta-lactams are no longer synergistic  IF high-level resistance to streptomycin is not detected, THEN report as streptomycin as effective for synergy purposes	High level resistance reflect production of ANT(6) or other enzymes or of ribosomal mutations. In vitro studies have shown lack of synergy of beta-lactams and gentamicin in such strains.	B	Zimmermann 1971
<b>Fluoroquinolones</b>							
4	<i>Enterococcus</i> spp.	norfloxacin screening test	ciprofloxacin levofloxacin	IF susceptible in the norfloxacin screening test THEN report susceptible to ciprofloxacin and levofloxacin  IF resistant in the norfloxacin screening test THEN report ciprofloxacin and levofloxacin resistant or test the desired agent individually.  NOTE: this rule applies to isolates from uncomplicated UTI only  IF the norfloxacin screening test is negative (susceptible) THEN report susceptible to ciprofloxacin and levofloxacin in isolates from uncomplicated/ localized UTI only.  IF the norfloxacin screening test is positive (resistant) THEN report isolates resistant to ciprofloxacin and levofloxacin.	As with other gram-positive organisms, first step mutants as well as overexpressed efflux pumps are detected with norfloxacin; therefore, norfloxacin-susceptible isolates can be reported as susceptible to the other fluoroquinolones. In most cases, a positive test in the screening test also indicates resistant to other fluoroquinolones.	C	Oyamada, et al., 2006
<b>Glycopeptides and lipoglycopeptides</b>							
5	<i>Enterococcus</i> spp.	vancomycin	dalbavancin oritavancin telavancin	IF susceptible to vancomycin THEN dalbavancin, oritavancin, telavancin as susceptible  IF resistant to vancomycin, determine the MIC and report dalbavancin, oritavancin and telavancin after consulting EUCAST guidance document "What to do when there are no breakpoints"	Dalbavancin, oritavancin and telavancin do not have breakpoints for enterococci; however, if for any reason the activity of the drugs towards enterococci needs to be known, the rule may provide guidance	C	Jones, et al., 2015; Mendes et al., 2015; Jones et al., 2015b

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5	<i>Enterococcus faecalis</i> <i>Enterococcus faecium</i>	vancomycin teicoplanin	teicoplanin	IF vancomycin resistant AND teicoplanin susceptible THEN report with a warning of resistance development to teicoplanin during therapy  IF vancomycin susceptible but <i>vanA</i> is detected by molecular methods THEN report resistant to vancomycin and teicoplanin;  IF vancomycin susceptible but <i>vanB</i> is detected by molecular methods THEN report resistant to vancomycin and add a warning of resistance development to teicoplanin during therapy	Enterococci harbouring <i>vanB</i> may appear susceptible to teicoplanin, but resistance may develop during therapy; the same is true if in phenotypically susceptible isolates harbour <i>vanA</i> or <i>vanB</i>	B	Holmes et al., 2013; Thaker et al., 2015
<b>Lincosamides</b>							
6	<i>Enterococcus faecium</i>	clindamycin	clindamycin	Do not report clindamycin as susceptible in <i>E. faecium</i>  IF clindamycin is tested THEN report as resistant irrespective of susceptibility testing result	Although isolates of <i>E. faecium</i> may appear susceptible <i>in vitro</i> the therapeutic utility of the drug is unknown in this species. Therefore, the result should be reported resistant or not at all. <i>E. faecium</i> that test resistant to clindamycin often express a <i>linB</i> gene  Although isolates of some <i>Enterococcus</i> species may appear active <i>in vitro</i> , MIC values are mostly high, clinical results unpredictable and reporting based on testing is discouraged.	C	Bozdogan et al., 1999

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

**References**

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