

Rule No.	Organisms	Indicator Agent	Agents affected	Rule	Remarks	Grade	References
Beta-lactams							
1	<i>Staphylococcus aureus</i>	cefoxitin screening for MRSA by MIC determination or disk diffusion.	All beta-lactams except those specifically licensed to treat infections caused by methicillin-resistant staphylococci expressing low affinity PBP2a	<p>IF resistant in the cefoxitin screening test (MRSA), THEN report resistant to all beta-lactams, except those specifically licensed to treat infections caused by methicillin-resistant staphylococci expressing low affinity PBP2a; such agents must be tested individually.</p> <p>IF susceptible in the cefoxitin screening test (MSSA), THEN report as susceptible to all beta-lactams with recognised anti-staphylococcal activity.</p> <p><i>EUCAST does not encourage the use of oxacillin for the screening for mecA/mecC mediated beta-lactam resistance in S. aureus.</i></p>	<p>Production of PBP2a leads to cross- resistance to beta-lactams. Ceftobiprole and ceftaroline are less affected by these changes than other beta-lactams and many MRSA isolates test susceptible.</p> <p>The specificity of oxacillin screening is poorer than for cefoxitin and other resistance mechanisms (hyperproduction of beta-lactamase) will influence the test result. The majority of "oxacillin positive" <i>S. aureus</i> will be <i>mecA</i>-positive, but some <i>mecC</i>-positive isolates will go undetected. Furthermore, some oxacillin-screen positive isolates (MIC-values of 4-8 mg/L) will have other beta-lactam resistance mechanisms than those mediated by <i>mec</i> genes (typically called BORSA, Borderline Oxacillin-Resistant <i>S. aureus</i>). EUCAST does not encourage screening for BORSA</p>	A	Chambers, Hackbarth, Drake, Rusnak, & Sande, 1984; Skov, Larsen, Kearns, Holmes, Teale, Edwards, Hill. 2014

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2	<i>Staphylococcus aureus</i>	benzylpenicillin (and beta-lactamase detection)	penicillins apart from isoxazoly-penicillins and combinations with beta-lactamase inhibitors	IF resistant to benzylpenicillin OR IF beta-lactamase is detected, THEN report as resistant to all penicillins, regardless of MIC, except the isoxazoly-penicillins and combinations with beta-lactamase inhibitors	Testing for beta-lactamase production with nitrocefin is discouraged. The appearance of the zone edge is more reliable, provided that the EUCAST-recommended benzylpenicillin 1U disk is used	C	Papanicolas et al., 2014 Hombach et al., 2017
Macrolides, lincosamides and streptogramins							
3	<i>Staphylococcus</i> spp.	erythromycin, clindamycin	clindamycin	<p>IF resistant to erythromycin AND susceptible to clindamycin, THEN test for inducible MLS_B resistance</p> <p>IF negative for inducibility, THEN report clindamycin susceptible</p> <p>IF positive for inducibility, THEN report clindamycin resistant.</p> <p>IF susceptible to erythromycin and clindamycin, THEN report as susceptible to all macrolides and lincosamides</p>	<p>Staphylococci resistant to macrolides but susceptible to clindamycin produce Erm-type ribosomal methylases conferring the inducible MLS_B phenotype, or express efflux pumps. In the case of inducible MLS_B resistance, constitutively resistant mutants can be selected by clindamycin.</p> <p>Adding a note may be considered, stating that clindamycin may still be used in less severe skin and soft tissue infections</p>	A	LaPlante, Leonard, Andes, Craig, & Rybak, 2008

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4	<i>Staphylococcus</i> spp.	erythromycin clindamycin	clindamycin	IF susceptible to erythromycin AND resistant to clindamycin THEN report as tested	Rare strains of staphylococci may produce an enzyme that inactivates lincosamides (<i>linA</i> or <i>InuA</i>) including clindamycin. The enzyme does not affect macrolides	C	Brisson-Noël, Delrieu, Samain, & Courvalin, 1988
Fluoroquinolones							
5	<i>Staphylococcus</i> spp.	norfloxacin screening test	all fluoroquinolones	IF susceptible in norfloxacin screening test, THEN report as susceptible to ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin IF resistant in norfloxacin screening test, THEN report individual agents as tested, and IF susceptible to either of ciprofloxacin, levofloxacin or moxifloxacin, THEN report agent as tested with a warning of risk for development of resistance during therapy with quinolones.	The screening test detects first step mutants and other mechanisms (e.g. efflux) that cause reduced susceptibility. Since mutants with increased efflux may still be susceptible to other fluoroquinolones these must be tested	C	Kaatz & Seo, 1997; Sierra et al., 2005
6	<i>Staphylococcus</i> spp.	Levofloxacin, moxifloxacin	all fluoroquinolones	IF resistant to levofloxacin or moxifloxacin, THEN report as resistant to all fluoroquinolones.	Acquisition of combined mutations in <i>grlA</i> and <i>gyrA</i> leads to complete or partial cross resistance to all fluoroquinolones.	C	Sierra et al., 2005
Tetracyclines							

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7	<i>Staphylococcus</i> spp.	tetracycline	doxycycline, minocycline, tigecycline	<p>IF susceptible to tetracycline, THEN report doxycycline, minocycline and tigecycline as susceptible.</p> <p>IF resistant to tetracycline, THEN EITHER report doxycycline and minocycline resistant OR determine the MIC of doxycycline and/or minocycline and report individually.</p> <p>Tigecycline must always be tested and reported individually</p>	<p>Tetracycline resistance in staphylococci is most often caused by TetK or TetM. Although TetM will cause resistance to all listed tetracyclines. TetL-harbouring isolates remain susceptible to minocycline.</p>	C	Trzcinski, Cooper, Hryniewicz, & Dowson, 2000
Glycopeptides and lipoglycopeptides							
8	<i>Staphylococcus</i> spp.	vancomycin	dalbavancin oritavancin telavancin	<p>IF susceptible to vancomycin THEN dalbavancin, oritavancin, telavancin can be reported as susceptible</p> <p>IF resistant to vancomycin, THEN report dalbavancin, oritavancin, telavancin as tested</p>	<p>Telavancin is licensed for suspected or proven infections with MRSA.</p>	C	Mendes, Farrell, Flamm, Sader, & Jones, 2015
Miscellaneous agents							
9	<i>Staphylococcus</i> spp.	linezolid	tedizolid	<p>IF susceptible to linezolid THEN tedizolid can be reported susceptible</p> <p>IF resistant to linezolid THEN report tedizolid as tested</p>	<p>Linezolid susceptible isolates may be reported tedizolid susceptible, although linezolid resistant isolates may be tedizolid susceptible</p>	C	Peñuelas et al., 2016

References

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