

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 the cefoxitin screening test is positive (resistant = MRSA), THEN report resistant to all beta-lactams, except those specifically licensed to treat infections caused by methicillin-resistant staphylococci expressing low affinity PBP2a (ceftaroline and ceftobiprole); such agents must be tested individually.</p> <p>IF the cefoxitin screening test is negative (susceptible = MSSA), THEN report as susceptible to all beta-lactams with recognised anti-staphylococcal activity.</p> <p>EUCAST does not encourage the use of oxacillin for the screening for <i>mecA/mecC</i> mediated beta-lactam resistance in <i>S. aureus</i>.</p>	<p>Production of PBP2a leads to cross- resistance to beta-lactams. Ceftaroline and ceftobiprole 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) but negative in the cefoxitin screen test 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, as there is no agreed action for situations when BORSA strains are detected.</p> <p>Occasionally, isolates with mutations in PBPs but lacking <i>mec</i> gene are detected (called MODSA – modified PBP <i>S. aureus</i> –). They might have borderline result in the cefoxitin and/or oxacillin screen tests. Epidemiology and clinical significance is unknown.</p>	A	Chambers, et al., 1984; Skov et al., 2014 Mlynarczyk-Bonikowska, et al., 2022

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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	IF resistant to erythromycin AND susceptible to clindamycin, THEN test for inducible MLS _B resistance IF negative for inducibility, THEN report clindamycin susceptible IF positive for inducibility, THEN report clindamycin resistant. IF susceptible to erythromycin and clindamycin, THEN report as susceptible to all macrolides and lincosamides	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. Adding a note may be considered, stating that clindamycin may still be used in less severe skin and soft tissue infections	A	LaPlante, et al., 2008
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>lnuA</i>) including clindamycin. The enzyme does not affect macrolides	C	Brisson-Noël, et al., 1988

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Fluoroquinolones							
5	<i>Staphylococcus</i> spp.	norfloxacin screening test	all fluoroquinolones	<p>IF the norfloxacin screening test is negative (susceptible) THEN report as "susceptible, increased exposure" to ciprofloxacin and levofloxacin, and "susceptible" to moxifloxacin.</p> <p>IF the norfloxacin screening test is positive (resistant), THEN report individual agents as tested</p> <p>IF the norfloxacin screening test is positive (resistant) AND "susceptible, increased exposure" to either of ciprofloxacin or levofloxacin or "susceptible" to moxifloxacin, THEN report agent as tested with a warning of risk for development of resistance during therapy with the agent</p>	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>griA</i> and <i>gyrA</i> leads to complete or partial cross resistance to all fluoroquinolones.	C	Sierra et al., 2005
Tetracyclines							
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. Tigecycline must always be tested and reported individually</p>	Tetracycline resistance in staphylococci is most often caused by TetK or TetM. Although TetM will cause resistance to all listed tetracyclines. TetL-harboured isolates remain susceptible to minocycline.	C	Trzcinski, et al., 2000

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Glycopeptides and lipoglycopeptides							
8	<i>Staphylococcus</i> spp.	vancomycin	dalbavancin oritavancin telavancin	IF susceptible to vancomycin THEN dalbavancin, oritavancin, telavancin can be reported as susceptible IF resistant to vancomycin, THEN report dalbavancin, oritavancin, telavancin as tested	Telavancin is licensed for suspected or proven infections with MRSA.	C	Mendes, Farrell, Flamm, Sader, & Jones, 2015
Miscellaneous agents							
8	<i>Staphylococcus</i> spp.	linezolid	tedizolid	IF susceptible to linezolid THEN tedizolid can be reported susceptible IF resistant to linezolid THEN report tedizolid as tested	Linezolid susceptible isolates may be reported tedizolid susceptible, although linezolid resistant isolates may be tedizolid susceptible	C	Peñuelas et al., 2016

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