

Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.

General Comments

For staphylococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, read the end point at the concentration in which there is ≈80% reduction in growth as compared to the control.

Historically, resistance to the penicillinase-stable penicillins has been referred to as “methicillin resistance” or “oxacillin resistance.” MRSAs are those strains of *S. aureus* that express *mecA* or another mechanism of methicillin resistance, such as changes in affinity of penicillin-binding proteins for oxacillin (modified *S. aureus* strains).

Most oxacillin resistance is mediated by *mecA*, encoding the PBP2a (also called PBP2'). Isolates that test positive for *mecA* or PBP2a should be **reported as** oxacillin resistant.

Oxacillin-resistant *S. aureus* and CoNS (MRS), are considered resistant to other β -lactam agents, ie, penicillins, β -lactam **combination agents, cephems** (with the exception of the cephalosporins with anti-MRSA activity), and carbapenems.

Routine testing of urine isolates of *Staphylococcus saprophyticus* is not advised, because infections respond to concentrations achieved in urine of antimicrobial agents commonly used to treat acute, uncomplicated UTIs (eg, nitrofurantoin, trimethoprim \pm sulfamethoxazole, or a fluoroquinolone).

General Comments

- (1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and no more than 6 disks on a 100-mm plate; disks should be placed no less than 24 mm apart, center to center (see M02,¹ Subchapter 3.6). Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see the *M02 Disk Diffusion Reading Guide*²). Hold the Petri plate a few inches above a black background illuminated with reflected light, except for linezolid, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter. For linezolid, any discernible growth within the zone of inhibition is indicative of resistance to the respective agent.
- (2) *S. aureus* complex consists of the coagulase-positive species *S. aureus*, *Staphylococcus argenteus*, and *Staphylococcus schweitzeri*. If *S. argenteus* is identified by MALDI-TOF MS or sequencing, it is recommended that it be reported as “*S. aureus* complex (*S. argenteus*),” and *S. aureus* phenotypic testing method recommendations, breakpoints, and interpretive categories should be used. Human infections with *S. schweitzeri* have yet to be reported.³

Most methicillin (oxacillin) resistance is mediated by *mecA*, encoding PBP2a (also called PBP2'). **Testing for *mecA* and PBP2a are the most definitive tests for detection of methicillin (oxacillin) resistance for *Staphylococcus* spp.** Isolates that test positive for *mecA* or PBP2a or resistant by any of the recommended phenotypic methods should be reported as methicillin (oxacillin) resistant (see Appendix H and table below).

Testing Conditions

Medium: Disk diffusion: MHA
Broth dilution: CAMHB; CAMHB + 2% NaCl for oxacillin;
CAMHB supplemented to 50 µg/mL calcium for daptomycin.
Agar dilution: MHA; MHA + 2% NaCl for oxacillin.
NOTE: Agar dilution has not been validated for daptomycin.

Inoculum: Colony suspension, equivalent to a 0.5 McFarland standard

Incubation: 35°C ± 2°C; ambient air
Disk diffusion: 16–18 hours; 24 hours (for cefoxitin when testing *Staphylococcus* spp., excluding *S. aureus*, *S. lugdunensis*, *S. pseudintermedius*, and *S. schleiferi*)
Dilution methods: 16–20 hours; 24 hours for oxacillin and vancomycin
Testing at temperatures above 35°C may not detect **methicillin (oxacillin)-resistant staphylococci (MRS)**.

Routine QC Recommendations (see Tables 4A-1 and 5A-1 for acceptable QC ranges)

Disk diffusion:
S. aureus ATCC®a 25923

Dilution methods:
S. aureus ATCC® 29213

Refer to Tables 4A-2 and 5A-2 to select strains for routine QC of β-lactam combination agents.

When a commercial test system is used for susceptibility testing, refer to the manufacturer's instructions for QC test recommendations and QC ranges.

| Organism | Phenotypic Methods for Detection of Methicillin (Oxacillin)-Resistant <i>Staphylococcus</i> spp. | | | | |
|--|--|--------------------------|-------------------------|--------------------------|---------------------|
| | Cefoxitin MIC | Cefoxitin disk diffusion | Oxacillin MIC | Oxacillin disk diffusion | Oxacillin salt agar |
| <i>S. aureus</i> | Yes (16-20 h) | Yes (16-18 h) | Yes (24 h) | No | Yes (24 h) |
| <i>S. lugdunensis</i> | Yes (16-20 h) | Yes (16-18 h) | Yes (24 h) | No | No |
| <i>S. epidermidis</i> | No | Yes (24 h) | Yes (24 h) | Yes (16-18 h) | No |
| <i>S. pseudintermedius</i> | No | No | Yes (24 h) | Yes (16-18 h) | No |
| <i>S. schleiferi</i> | No | No | Yes (24 h) | Yes (16-18 h) | No |
| <i>Staphylococcus</i> spp. (not listed above or not identified to the species level) | No | Yes ^a (24 h) | Yes ^a (24 h) | No | No |

Table 2C. *Staphylococcus* spp. (Continued)

| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|---|---------------------------------|--------------|---|-----|---|------|--|-----|---|--------|--|
| | | | S | SDD | I | R | S | SDD | I | R | |
| PENICILLINASE-LABILE PENICILLINS | | | | | | | | | | | |
| <p>(10) Penicillin-susceptible staphylococci are susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections (including both penicillinase-labile and penicillinase-stable agents; see Glossary I). Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins.</p> <p>(11) Penicillin should be used to test the susceptibility of all staphylococci to penicillinase-labile penicillins (see Glossary I). Penicillin-resistant strains of staphylococci produce β-lactamase. Perform a test(s) to detect β-lactamase production on staphylococci for which the penicillin MICs are ≤ 0.12 µg/mL or zone diameters ≥ 29 mm before reporting the isolate as penicillin susceptible. Rare isolates of staphylococci that contain genes for β-lactamase production may appear negative by β-lactamase tests. Consequently, for serious infections requiring penicillin therapy, laboratories should perform MIC tests and β-lactamase testing on all subsequent isolates from the same patient. PCR testing of the isolate for the <i>blaZ</i> β-lactamase gene may be considered. See Table 3F.</p> | | | | | | | | | | | |
| Penicillin | All staphylococci | 10 units | ≥ 29 | - | - | ≤ 28 | ≤ 0.12 | - | - | ≥ 0.25 | (12) For MRS, report penicillin as resistant or do not report. |
| PENICILLINASE-STABLE PENICILLINS | | | | | | | | | | | |
| <p>(13) Cefoxitin is tested as a surrogate for oxacillin for some species of <i>Staphylococcus</i>. Isolates that test resistant by cefoxitin or oxacillin, when using the appropriate test method for the species, should be reported as methicillin (oxacillin) resistant. If testing only cefoxitin, report as methicillin (oxacillin) susceptible or resistant based on the cefoxitin result.</p> <p>(14) Oxacillin (or cefoxitin) results can be applied to the other penicillinase-stable penicillins (cloxacillin, dicloxacillin, methicillin, and nafcillin). For agents with established clinical efficacy and considering site of infection and appropriate dosing, methicillin (oxacillin)-susceptible staphylococci can be considered susceptible to:</p> <ul style="list-style-type: none"> • β-lactam combination agents (amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam) • Oral cepheims (cefaclor, cefdinir, cephalexin, cefpodoxime, cefprozil, cefuroxime, loracarbef) • Parenteral cepheims including cephalosporins I, II, III, and IV (cefamandole, cefazolin, cefepime, cefmetazole, cefonicid, cefoperazone, cefotaxime, cefotetan, ceftizoxime, ceftriaxone, cefuroxime, ceftaroline, moxalactam) • Carbapenems (doripenem, ertapenem, imipenem, meropenem) <p><u>Methicillin (oxacillin)-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of ceftaroline. Thus, susceptibility or resistance to a wide array of β-lactam antimicrobial agents may be deduced from testing only penicillin and either cefoxitin or oxacillin. Testing of other β-lactam agents, except ceftaroline, is not advised. See general comments (7) and (8).</u></p> <p>Additional explanation on the use of cefoxitin for prediction of <i>mecA</i>-mediated methicillin (oxacillin) resistance can be found in Subchapter 3.12 of M07⁴ and Subchapter 3.9 of M02.¹</p> | | | | | | | | | | | |

Table 2C. *Staphylococcus* spp. (Continued)




| Antimicrobi al Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|--|--|---|------------|------------|--|--|------------|------------|--|--|
| | | | S | SDD | I | R | S | SDD | I | R | |
| PENICILLINASE-STABLE PENICILLINS (Continued) | | | | | | | | | | | |
| Oxacillin  | S. aureus and S. lugdunensis  | - 30 µg cefoxitin (surrogate test for oxacillin)  | - ≥ 22 | - - | - - | - ≤ 21 | ≤ 2 (oxacillin) ≤ 4 (cefoxitin) | - - | - - | ≥ 4 (oxacillin) ≥ 8 (cefoxitin) | (15) Oxacillin disk testing is not reliable for S. aureus and S. lugdunensis. (16) For isolates of S. aureus that do not grow well on CAMHB or unsupplemented MHA (eg, small-colony variants), testing on other media (eg, BMHA) does not reliably detect mecA-mediated resistance. Testing for PBP2a using induced growth (ie, growth taken from the zone margin surrounding a cefoxitin disk on either BMHA or a blood agar plate after 24 hours incubation in 5% CO2) or mecA should be done. See general comments (7) and (8) and comments (10), (13), and (14). |
| Oxacillin | S. epidermidis | 1 µg oxacillin 30 µg cefoxitin (surrogate test for oxacillin) | ≥ 18 (oxacillin) ≥ 25 (cefoxitin) | - - | - - | ≤ 17 (oxacillin) ≤ 24 (cefoxitin) | ≤ 0.5 (oxacillin) - | - - | - - | ≥ 1 (oxacillin) - | See general comments (7) and (8) and comments (10), (13), and (14). (17) Cefoxitin MIC testing is not reliable for detecting mecA-mediated resistance in S. epidermidis. |
| | S. pseudintermedius and S. schleiferi | 1 µg oxacillin | ≥ 18 | - | - | ≤ 17 | ≤ 0.5 | - | - | ≥ 1 | (18) Neither cefoxitin MIC nor cefoxitin disk tests are reliable for detecting mecA-mediated resistance in S. pseudintermedius and S. schleiferi. See general comments (7) and (8) and comments (10), (13), and (14). |

Table 2C. *Staphylococcus* spp. (Continued)


| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|---|---|---|-------|---|------------------|--|-----|---|-----------------|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| PENICILLINASE-STABLE PENICILLINS (Continued) | | | | | | | | | | | |
| Oxacillin | Staphylococcus spp., except: S. aureus S. lugdunensis S. epidermidis S. pseudintermedius S. schleiferi | 30 µg cefoxitin (surrogate test for oxacillin)  | ≥ 25 (cefoxitin) | - | - | ≤ 24 (cefoxitin) | ≤ 0.5 (oxacillin) | - | - | ≥ 1 (oxacillin) | (19) Oxacillin MIC breakpoints may overcall resistance, and some isolates for which the oxacillin MICs are 1-2 µg/mL may be mecA negative. Isolates from serious infections for which oxacillin MICs are 1-2 µg/mL may be tested for mecA or for PBP2a. Isolates that test mecA or PBP2a negative should be reported as methicillin (oxacillin) susceptible. See general comments (7) and (8) and comments (10), (13), and (14). |
| CEPHEMS (PARENTERAL) | | | | | | | | | | | |
| Ceftaroline | S. aureus, including MRSA | 30 µg | ≥ 25 | 20-24 | | ≤ 19 | ≤ 1 | 2-4 | - | ≥ 8 | (20) The breakpoint for susceptible is based on a dosage regimen of 600 mg administered every 12 h. (21) The breakpoint for SDD is based on a dosage of 600 mg every 8 h administered over 2 h. |

Table 2C. *Staphylococcus* spp. (Continued)

| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|---|--|--------------|---|-----|---|---|--|-----|------|-----|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| GLYCOPEPTIDES | | | | | | | | | | | |
| (22) MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin. The disk test does not differentiate vancomycin-susceptible isolates of <i>S. aureus</i> from vancomycin-intermediate isolates, nor does the test differentiate among vancomycin-susceptible, -intermediate, and -resistant isolates of <i>Staphylococcus</i> spp. other than <i>S. aureus</i> , all of which give similar size zones of inhibition. | | | | | | | | | | | |
| Vancomycin | <i>S. aureus</i> , including MRSA | - | - | - | - | - | ≤2 | - | 4-8 | ≥16 | (23) For <i>S. aureus</i> , vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy. (24) Send any <i>S. aureus</i> for which the vancomycin is ≥8 µg/mL to a referral laboratory. See Appendix A. Also refer to Table 3G-1 for <i>S. aureus</i> , Subchapter 3.12 in M07, ⁴ and Subchapter 3.9 in M02. ¹ |
| | <i>Staphylococcus</i> spp. other than <i>S. aureus</i> | - | - | - | - | - | ≤4 | - | 8-16 | ≥32 | (25) Send any <i>Staphylococcus</i> spp. other than <i>S. aureus</i> for which the vancomycin MIC is ≥32 µg/mL to a referral laboratory. See Appendix A. See also Subchapter 3.12 in M07 ⁴ and Subchapter 3.9 in M02. ¹ |
| LIPOGLYCOPEPTIDES | | | | | | | | | | | |
| Dalbavancin | <i>S. aureus</i> , including MRSA | - | - | - | - | - | ≤0.25 | - | - | - | (26) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes. |
| Oritavancin | | - | - | - | - | - | ≤0.12 | - | - | - | (27) Breakpoints are based on a dosage regimen of 1200 mg IV administered once. |
| Telavancin | | - | - | - | - | - | ≤0.12 | - | - | - | (28) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h. |
| Teicoplanin (Inv.) | All staphylococci | - | - | - | - | - | ≤8 | - | 16 | ≥32 | |

Table 2C. *Staphylococcus* spp. (Continued)

| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|---------------------------------|--------------|---|-----|-------|------|--|-----|-----|------|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| LIPOPEPTIDES | | | | | | | | | | | |
| Daptomycin | All staphylococci | - | - | - | - | - | ≤1 | - | - | - | (29) Not routinely reported on organisms isolated from the respiratory tract. |
| AMINOGLYCOSIDES | | | | | | | | | | | |
| (30) For staphylococci that test susceptible, gentamicin is used only in combination with other active agents that test susceptible. | | | | | | | | | | | |
| Gentamicin | All staphylococci | 10 µg | ≥ 15 | - | 13-14 | ≤ 12 | ≤ 4 | - | 8 | ≥ 16 | |
| MACROLIDES | | | | | | | | | | | |
| (31) Not routinely reported on organisms isolated from the urinary tract. | | | | | | | | | | | |
| Azithromycin or clarithromycin or erythromycin | All staphylococci | 15 µg | ≥ 18 | - | 14-17 | ≤ 13 | ≤ 2 | - | 4 | ≥ 8 | |
| | | 15 µg | ≥ 18 | - | 14-17 | ≤ 13 | ≤ 2 | - | 4 | ≥ 8 | |
| | | 15 µg | ≥ 23 | - | 14-22 | ≤ 13 | ≤ 0.5 | - | 1-4 | ≥ 8 | |
| Dirithromycin* | | 15 µg | ≥ 19 | - | 16-18 | ≤ 15 | ≤ 2 | - | 4 | ≥ 8 | |
| TETRACYCLINES | | | | | | | | | | | |
| (32) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both. | | | | | | | | | | | |
| Tetracycline | All staphylococci | 30 µg | ≥ 19 | - | 15-18 | ≤ 14 | ≤ 4 | - | 8 | ≥ 16 | |
| Doxycycline | | 30 µg | ≥ 16 | - | 13-15 | ≤ 12 | ≤ 4 | - | 8 | ≥ 16 | |
| Minocycline | | 30 µg | ≥ 19 | - | 15-18 | ≤ 14 | ≤ 4 | - | 8 | ≥ 16 | |
| FLUOROQUINOLONES | | | | | | | | | | | |
| (33) Staphylococcus spp. may develop resistance during prolonged therapy with quinolones. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted. | | | | | | | | | | | |
| Ciprofloxacin or levofloxacin | All staphylococci | 5 µg | ≥ 21 | - | 16-20 | ≤ 15 | ≤ 1 | - | 2 | ≥ 4 | |
| Moxifloxacin | | 5 µg | ≥ 19 | - | 16-18 | ≤ 15 | ≤ 1 | - | 2 | ≥ 4 | |
| | | 5 µg | ≥ 24 | - | 21-23 | ≤ 20 | ≤ 0.5 | - | 1 | ≥ 2 | |
| Enoxacin* (U) ^b | | 10 µg | ≥ 18 | - | 15-17 | ≤ 14 | ≤ 2 | - | 4 | ≥ 8 | |
| Gatifloxacin* | | 5 µg | ≥ 23 | - | 20-22 | ≤ 19 | ≤ 0.5 | - | 1 | ≥ 2 | |
| Grepafloxacin* | | 5 µg | ≥ 18 | - | 15-17 | ≤ 14 | ≤ 1 | - | 2 | ≥ 4 | |
| Lomefloxacin* | | 10 µg | ≥ 22 | - | 19-21 | ≤ 18 | ≤ 2 | - | 4 | ≥ 8 | |
| Norfloxacin* (U) ^b | | 10 µg | ≥ 17 | - | 13-16 | ≤ 12 | ≤ 4 | - | 8 | ≥ 16 | |
| Ofloxacin* | | 5 µg | ≥ 18 | - | 15-17 | ≤ 14 | ≤ 1 | - | 2 | ≥ 4 | |
| Sparfloxacin* | | 5 µg | ≥ 19 | - | 16-18 | ≤ 15 | ≤ 0.5 | - | 1 | ≥ 2 | |
| Fleroxacin (Inv.) | | 5 µg | ≥ 19 | - | 16-18 | ≤ 15 | ≤ 2 | - | 4 | ≥ 8 | |

Table 2C. *Staphylococcus* spp. (Continued)

| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|---------------------------------|---------------------------------|---------------|---|-----|-------|------|--|-----|-----|--------|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| NITROFURANS | | | | | | | | | | | |
| Nitrofurantoin (U) ^b | All staphylococci | 300 µg | ≥ 17 | - | 15-16 | ≤ 14 | ≤ 32 | - | 64 | ≥ 128 | |
| LINCOSAMIDES | | | | | | | | | | | |
| Clindamycin | All staphylococci | 2 µg | ≥ 21 | - | 15-20 | ≤ 14 | ≤ 0.5 | - | 1-2 | ≥ 4 | (34) For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin (see Table 3I, Subchapter 3.9 in M02, ¹ and Subchapter 3.12 in M07 ⁴). See comment (31). |
| FOLATE PATHWAY ANTAGONISTS | | | | | | | | | | | |
| Trimethoprim-sulfamethoxazole | All staphylococci | 1.25/23.75 µg | ≥ 16 | - | 11-15 | ≤ 10 | ≤ 2/38 | - | - | ≥ 4/76 | |
| Sulfonamides (U) ^b | All staphylococci | 250 or 300 µg | ≥ 17 | - | 13-16 | ≤ 12 | ≤ 256 | - | - | ≥ 512 | (35) Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations. |
| Trimethoprim (U) ^b | All staphylococci | 5 µg | ≥ 16 | - | 11-15 | ≤ 10 | ≤ 8 | - | - | ≥ 16 | |
| PHENICOLS | | | | | | | | | | | |
| Chloramphenicol* | All staphylococci | 30 µg | ≥ 18 | - | 13-17 | ≤ 12 | ≤ 8 | - | 16 | ≥ 32 | See comment (31). |
| ANSAMYCINS | | | | | | | | | | | |
| Rifampin | All staphylococci | 5 µg | ≥ 20 | - | 17-19 | ≤ 16 | ≤ 1 | - | 2 | ≥ 4 | (36) Rx: Rifampin should not be used alone for antimicrobial therapy. |
| STREPTOGRAMINS | | | | | | | | | | | |
| Quinupristin-dalfopristin* | S. aureus | 15 µg | ≥ 19 | - | 16-18 | ≤ 15 | ≤ 1 | - | 2 | ≥ 4 | (37) Report only on methicillin (oxacillin)-susceptible S. aureus. |



Table 2C. *Staphylococcus* spp. (Continued)

| Antimicrobial Agent | Staphylococcus spp. Indications | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|---------------------------------|--------------|---|-----|---|-----|--|-----|---|----|--|
| | | | S | SDD | I | R | S | SDD | I | R | |
| OXAZOLIDINONES | | | | | | | | | | | |
| (38) S. aureus that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that test resistant to linezolid may be susceptible to tedizolid. | | | | | | | | | | | |
| Linezolid | All staphylococci | 30 µg | ≥21 | - | - | ≤20 | ≤ 4 | - | - | ≥8 | (39) When testing linezolid, disk diffusion zones should be examined using transmitted light. Organisms with resistant results by disk diffusion should be confirmed using an MIC method. |
| Tedizolid | S. aureus, including MRSA | - | - | - | - | - | ≤0.5 | - | 1 | ≥2 | (40) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h. |
| PLEUROMUTILINS | | | | | | | | | | | |
| Lefamulin | S. aureus, including MRSA | 20 µg | ≥23 | - | - | - | ≤0.25 | - | - | - | (41) The breakpoints for susceptible are based on a dosage regimen of 150 mg IV or 600 mg orally administered every 12 h. (42) Not routinely reported on organisms isolated from the urinary tract. |

Abbreviations: ATCC®, American Type Culture Collection; BMHA, blood Mueller-Hinton agar; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; ICR, inducible clindamycin resistance; **Inv.**, **investigational agent**; IV, intravenous; MALDI-TOF MS; matrix-assisted laser-desorption/ionization time-of-flight mass spectrometry; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant staphylococci; MRSA, methicillin (oxacillin)-resistant *S. aureus*; PBP2a, penicillin-binding protein 2a; PCR, polymerase chain reaction; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent; **U, urine**; UTI, urinary tract infection.

Symbol: *, designation for “Other” agents that are not included in Tables 1 but have established clinical breakpoints.

دوره سی و سوم – تابستان 1398
تعداد آزمایشگاهها 1700
استافیلوکوک کواگولاز منفی کشت ادرار

| Antibiotic | No Lab incorrect used |
|----------------|-----------------------|
| Cefazolin | 112 |
| Cefixime | 175 |
| Cefotaxim | 153 |
| Ceftazidim | 63 |
| Ceftriaxon | 230 |
| Ceftizoxim | 67 |
| Doxycyclin | 134 |
| Imipenem | 98 |
| Kanamycin | 12 |
| Nalidixic acid | 141 |
| Rifampin | 59 |
| Tetracyclin | 418 |

دوره سی و هفتم – پاییز 1399
استافیلوکوک کشت زخم

| Antibiotic | No Lab incorrect used |
|-----------------------|------------------------------|
| Cefazolin | 142 |
| Cefixime | 162 |
| Cefotaxim | 119 |
| Ceftriaxon | 230 |
| Levofloxacin | 109 |
| Nalidixic acid | 95 |
| Nitrofurantoin | 502 |
| Norfloxacin | 119 |
| Ofloxacin | 126 |
| Vancomycin | 466 |

Zone Diameter and MIC Breakpoints for *Enterococcus* spp.

General Comments

WARNING: For *Enterococcus* spp., **aminoglycosides** (except for high-level resistance testing), **cephalosporins**, **clindamycin**, and **trimethoprim-sulfamethoxazole** may appear active *in vitro*, but they are not effective clinically, and isolates should not be reported as susceptible.

Synergy between ampicillin, penicillin, or vancomycin and an aminoglycoside can be predicted for enterococci by using a high-level aminoglycoside (gentamicin and streptomycin) test

Intermediate ranges denoted with a “^” for the applicable antimicrobial agents in the drug groups in Tables 2 are based on the known ability of these agents to concentrate in the urine; some agents may also have the potential to concentrate at other anatomical sites (eg, epithelial lining).

Table 2D. *Enterococcus* spp. (Continued)

| Antimicrobial Agent | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--------------------------|-------------------|---|--------|--------------|--|--------|--------|--------------|---|
| | | S | I | R | S | SDD | I | R | |
| PENICILLINS | | | | | | | | | |
| Penicillin Ampicillin | 10 units 10 µg | ≥ 15 ≥ 17 | - - | ≤ 14 ≤ 16 | ≤ 8 ≤ 8 | - - | - - | ≥ 16 ≥ 16 | <p>(7) The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. Ampicillin results may be used to predict susceptibility to amoxicillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam among non-β-lactamase-producing enterococci. Ampicillin susceptibility can be used to predict imipenem susceptibility, providing the species is confirmed to be <i>E. faecalis</i>.</p> <p>(8) Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, and piperacillin-tazobactam for non-β-lactamase-producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, testing of penicillin is required.</p> <p>(9) Rx: Combination therapy with high-dosage parenteral ampicillin, amoxicillin, penicillin, or vancomycin (for susceptible strains only), plus an aminoglycoside, is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of enterococci.</p> <p>(10) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h.</p> <p>(11) Breakpoints when oral ampicillin is used for therapy of uncomplicated UTIs only are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h.</p> |

Table 2D. *Enterococcus* spp. (Continued)

| Antimicrobial Agent | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--------------------------|-------------------|---|--------|--------------|--|--------|--------|--------------|--|
| | | S | I | R | S | SDD | I | R | |
| PENICILLINS (Continued) | | | | | | | | | |
| Penicillin Ampicillin | 10 units 10 µg | ≥ 15 ≥ 17 | - - | ≤ 14 ≤ 16 | ≤ 8 ≤ 8 | - - | - - | ≥ 16 ≥ 16 | (12) Penicillin or ampicillin resistance among enterococci due to B-lactamase production has been reported very rarely. Penicillin or ampicillin resistance due to B-lactamase production is not reliably detected with routine disk or dilution methods but is detected using a direct, nitrocefin-based B-lactamase test. Because of the rarity of B-lactamase-positive enterococci, this test does not need to be performed routinely but can be used in selected cases. A positive B-lactamase test predicts resistance to penicillin as well as amino- and ureidopenicillins (see Glossary I). |
| GLYCOPEPTIDES | | | | | | | | | |
| Vancomycin | 30 µg | ≥ 17 | 15-16 | ≤ 14 | ≤ 4 | - | 8-16 | ≥ 32 | (13) When testing vancomycin against enterococci, plates should be held a full 24 hours for accurate detection of resistance. Zones should be examined using transmitted light; the presence of a haze or any growth within the zone of inhibition indicates resistance. <u>Organisms with intermediate zones</u> should be tested by an MIC method as described in M07. ³ For isolates for which the vancomycin MICs are 8-16 µg/mL, perform biochemical tests for identification as listed under the “Vancomycin MIC ≥ 8 µg/mL” test found in Table 3H. See general comment (5) and comment (9). |

Table 2D. *Enterococcus* spp. (Continued)

| Antimicrobial Agent | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|--------------|---|-------|-----|--|-----|----|-----|---|
| | | S | I | R | S | SDD | I | R | |
| LIPOGLYCOPEPTIDES | | | | | | | | | |
| Dalbavancin | - | - | - | - | ≤0.25 | - | - | - | (14) Report only on vancomycin-susceptible <i>E. faecalis</i> . (15) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes. |
| Oritavancin | - | - | - | - | ≤0.12 | - | - | - | (16) Breakpoints are based on a dosage regimen of 1200 mg administered IV once. See comment (14). |
| Telavancin | - | - | - | - | ≤0.25 | - | - | - | (17) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h. See comment (14). |
| Teicoplanin (Inv.) | 30 µg | ≥14 | 11-13 | ≤10 | ≤8 | - | 16 | ≥32 | |
| LIPOPEPTIDES | | | | | | | | | |
| Daptomycin <i>E. faecium</i> only | - | - | - | - | - | ≤4 | - | ≥8 | (18) Not routinely reported on organisms isolated from the respiratory tract. (19) The breakpoint for SDD is based on a dosage regimen of 8-12 mg/kg administered every 24 h and is intended for serious infections due to <i>E. faecium</i> . Consultation with an infectious diseases specialist is recommended. |
| Daptomycin <i>Enterococcus</i> spp. other than <i>E. faecium</i> | - | - | - | - | ≤2 | - | 4 | ≥8 | (20) The breakpoint for susceptible is based on a dosage regimen of 6 mg/kg administered every 24 h. See comment (18). |

Table 2D. *Enterococcus* spp. (Continued)


| Antimicrobial Agent | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|---|--------------|---|--------------------|-----|--|-----|----------------|------|---|
| | | S | I | R | S | SDD | I | R | |
| MACROLIDES | | | | | | | | | |
| Erythromycin* | 15 µg | ≥23 | 14-22 | ≤13 | ≤0.5 | - | 1-4 | ≥8 | (21) Not routinely reported on organisms isolated from the urinary tract. |
| TETRACYCLINES | | | | | | | | | |
| (22) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both. | | | | | | | | | |
| Tetracycline (U) ^b | 30 µg | ≥19 | 15-18 | ≤14 | ≤4 | - | 8 | ≥16 | |
| Doxycycline* | 30 µg | ≥16 | 13-15 | ≤12 | ≤4 | - | 8 | ≥16 | |
| Minocycline* | 30 µg | ≥19 | 15-18 | ≤14 | ≤4 | - | 8 | ≥16 | |
| FLUOROQUINOLONES | | | | | | | | | |
| Ciprofloxacin (U) ^b | 5 µg | ≥21 | 16-20 [^] | ≤15 | ≤1 | - | 2 [^] | ≥4 | |
| Levofloxacin (U) ^b | 5 µg | ≥17 | 14-16 [^] | ≤13 | ≤2 | - | 4 [^] | ≥8 | |
| Gatifloxacin* | 5 µg | ≥18 | 15-17 [^] | ≤14 | ≤2 | - | 4 [^] | ≥8 | |
| Norfloxacin* (U) ^b | 10 µg | ≥17 | 13-16 | ≤12 | ≤4 | - | 8 | ≥16 | |
| NITROFURANS | | | | | | | | | |
| Nitrofurantoin (U) ^b | 300 µg | ≥17 | 15-16 | ≤14 | ≤32 | - | 64 | ≥128 | |
| ANSAMYCINS | | | | | | | | | |
| Rifampin* | 5 µg | ≥20 | 17-19 | ≤16 | ≤1 | - | 2 | ≥4 | (23) Rx: Rifampin should not be used alone for antimicrobial therapy.  |
| FOSFOMYCINS | | | | | | | | | |
| Fosfomycin (U) ^b | 200 µg | ≥16 | 13-15 | ≤12 | ≤64 | - | 128 | ≥256 | (24) Report only on <i>E. faecalis</i> . (25) The approved MIC testing method is agar dilution. Agar media should be supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution testing should not be performed. (26) The 200-µg fosfomycin disk contains 50 µg glucose-6-phosphate. |

Table 2D. *Enterococcus* spp. (Continued)

| Antimicrobial Agent | Disk Content | Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm | | | Interpretive Categories and MIC Breakpoints, µg/mL | | | | Comments |
|--|--------------|---|-------|------|--|-----|----|------|---|
| | | S | I | R | S | SDD | I | R | |
| PHENICOLS | | | | | | | | | |
| Chloramphenicol* | 30 µg | ≥ 18 | 13-17 | ≤ 12 | ≤ 8 | - | 16 | ≥ 32 | See comment (21). |
| STREPTOGRAMINS | | | | | | | | | |
| Quinupristin-dalfopristin* | 15 µg | ≥ 19 | 16-18 | ≤ 15 | ≤ 1 | - | 2 | ≥ 4 | (27) Report only on vancomycin-resistant <i>E. faecium</i> . |
| OXAZOLIDINONES | | | | | | | | | |
| (28) <i>E. faecalis</i> that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that are intermediate or resistant to linezolid may be susceptible to tedizolid. | | | | | | | | | |
| Linezolid | 30 µg | ≥ 23 | 21-22 | ≤ 20 | ≤ 2 | - | 4 | ≥ 8 | |
| Tedizolid | - | - | - | - | ≤ 0.5 | - | - | - | (29) Report only on <i>E. faecalis</i> . (30) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h. |

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; **Inv.**, investigational agent; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent; **U**, urine; UTI, urinary tract infection.

Symbols: ^, designation for agents that have the potential to concentrate in the urine; *, designation for “Other” agents not included in Tables 1 but have established clinical breakpoints.

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