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# Update of the Telavancin Activity *In Vitro* Tested Against a Worldwide Collection of Gram-Positive Clinical Isolates (2013) When Applying the Revised Susceptibility Testing Method

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## ABSTRACT

**Background.** The broth microdilution method for telavancin was recently revised by the FDA and CLSI. This study assessed the telavancin activity using the revised method that uses dimethyl sulfoxide as solvent and diluent for stock solution preparation and dilution for panel production, following CLSI guidelines for water-insoluble agents. Polysorbate-80 was also added in the test medium. This revised method was deemed necessary for greater accuracy and reproducibility of telavancin MIC results.

**Methods.** A total of 12,346 isolates were collected from 90 sites, as part of the telavancin International Surveillance Program for the Americas, Europe, and Asia-Pacific. Organism identification was performed by standard algorithms and MALDI-TOF. Susceptibility testing was performed by CLSI methods (M07-A9 and M100-S24). MIC interpretation was guided by FDA (telavancin), EUCAST (2014), and CLSI (2014) criteria.

**Results.** Telavancin had $MIC_{50}$ and $MIC_{90}$ values of 0.03 and 0.06 µg/mL against staphylococci, respectively, regardless of methicillin susceptibility. Telavancin inhibited all *S. aureus* at the revised FDA breakpoint for susceptibility (≤0.12 µg/mL). Telavancin was 8-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL), and 16- to 32-fold more active than vancomycin ($MIC_{50/90}$, 1/1 µg/mL) and linezolid ($MIC_{50/90}$, 1/1 µg/mL) against methicillin-resistant *S. aureus*. All vancomycin-susceptible *E. faecalis* were inhibited by telavancin ($MIC_{50/90}$, 0.12/0.12 µg/mL) at ≤0.25 µg/mL (FDA breakpoint for susceptibility), except for 1 strain (MIC, 0.5 µg/mL). *E. faecalis* with telavancin MIC values of >1 µg/mL had a VanA resistance phenotype. Based on $MIC_{50}$, telavancin was ≥8-fold more potent than comparators against vancomycin-susceptible *E. faecalis*. Vancomycin-susceptible *E. faecium* showed low telavancin MIC results ($MIC_{50/90}$, ≤0.015/0.03 µg/mL), while VanA isolates had higher values (≥0.25 µg/mL). Streptococci showed telavancin $MIC_{50}$ of ≤0.015 µg/mL and $MIC_{90}$ of ≤0.015 to 0.03 µg/mL, except for *S. agalactiae* ($MIC_{50/90}$, 0.03/0.03 µg/mL).

**Conclusion.** Telavancin exhibited greater potency than comparators when tested against this contemporary and worldwide collection of organisms. These *in vitro* results obtained by a newly revised broth microdilution method establish the new benchmark of telavancin activity worldwide, as this replaces the previous susceptibility testing.

## INTRODUCTION

- The lipoglycopeptide telavancin possesses bactericidal activity against clinically relevant Gram-positive pathogens, such as *Staphylococcus aureus*, including methicillin-resistant (MRSA) isolates, vancomycin-intermediate and heterogeneous vancomycin-intermediate isolates, streptococci, and vancomycin-susceptible enterococci.
- This bactericidal activity derives from a dual mechanism of action consisting of inhibition of peptidoglycan biosynthesis, similar to the glycopeptides, as well as interaction with the bacterial membrane to affect changes in membrane permeability and depolarization.
- Early in 2014, a revised broth microdilution susceptibility testing method for telavancin was published in the Clinical and Laboratory Standards Institute (CLSI) M100-S24 document[1] and approved by the U.S. Food and Drug Administration (FDA), followed by the release of a labeling supplement for VIBATIV® (telavancin for injection).[2]
  - This revised susceptibility testing method follows the CLSI guidelines for water-insoluble agents and consists of the use of dimethyl sulfoxide as solvent for stock solution preparation and as a diluent for dilution of stock solution when manufacturing 96-well minimum inhibitory concentration (MIC) plates.[3]
  - This method is consistent with those applied to other members of the lipoglycopeptide class (ie, oritavancin and dalbavancin), which include the addition of polysorbate-80 (P-80; 0.002%) to the test medium. This approach mitigates the lipoglycopeptide propensity to bind to plastic.[4,5]
- This study was conducted to assess and update the activity of telavancin against a worldwide contemporary collection of clinical isolates using the recently approved broth microdilution method.

## MATERIALS AND METHODS

### Bacterial strain collection

- A total of 12,346 consecutive, non-duplicate Gram-positive clinical isolates were included in this study, which were collected from 90 centers in the Americas, Europe, and Asia-Pacific (APAC) regions.
- These isolates were recovered from blood (2,739; 22.2%); skin and skin structure infections (4,243; 34.4%); and from patients with community- (1,401; 11.3%) and hospital-acquired pneumonia (1,821; 14.7%), urinary tract infections (458; 3.7%), intra-abdominal infections (419; 3.4%), and other less prevalent or undetermined infection sources (1,265; 10.2%).
- Isolates were determined to be clinically significant based on local guidelines and were submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, IA, USA), as part of the SENTRY Antimicrobial Surveillance Program during 2013. Isolates were initially identified by the participating laboratory and identification confirmed by the reference monitoring laboratory by standard algorithms and supported by MALDI-TOF-MS (Bruker Daltonics, Bremen, Germany).

**Table 1. Antimicrobial activity and MIC distribution for telavancin when tested against contemporary (2013) worldwide collection of clinical isolates using a recently approved revised BMD susceptibility testing method**

| | MIC (µg/mL) | | No. (cumulative %) inhibited at telavancin MIC (µg/mL)[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Organism[a] (no. tested)** | **50%** | **90%** | **≤0.015** | **0.03** | **0.06** | **0.12** | **0.25** | **0.5** | **1** | **2** | **>2** |
| *S. aureus* (6,843) | 0.03 | 0.06 | 324 (4.7) | **4,741 (74.0)** | 1,770 (99.9) | 8 (100.0) | – | – | – | – | – |
| MSSA (4,230) | 0.03 | 0.06 | 241 (5.7) | **2,931 (75.0)** | 1,056 (>99.9) | 2 (100.0) | – | – | – | – | – |
| MRSA (2,613) | 0.03 | 0.06 | 83 (3.2) | **1,810 (72.4)** | 714 (99.8) | 6 (100.0) | – | – | – | – | – |
| CoNS (875) | 0.03 | 0.06 | 153 (17.5) | 310 (52.9) | **397 (98.3)** | 13 (99.8) | 2 (100.0) | – | – | – | – |
| *E. faecalis* (702) | 0.12 | 0.12 | 2 (0.3) | 20 (3.1) | 228 (35.6) | **431 (97.0)** | 10 (98.4) | 1 (98.6) | 0 (98.6) | 2[b] (98.9) | 8[c] (100.0) |
| *E. faecium* (437) | 0.03 | 2 | **156 (35.7)** | 72 (52.2) | 9 (54.2) | 1 (54.5) | 8 (56.3) | 39 (65.2) | 79 (83.3) | 57 (96.3) | 16 (100.0) |
| Vancomycin-susceptible (228) | ≤0.015 | 0.03 | **149 (65.4)** | 70 (96.1) | 8 (99.6) | 1 (100.0) | – | – | – | – | – |
| VanA (196) | 1 | 2 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 5 (2.6) | 39 (22.4) | **79 (62.8)** | 57 (91.8) | 16 (100.0) |
| VanB (13) | ≤0.015 | 0.25 | 7 (53.8) | 2 (69.2) | 1 (76.9) | 0 (76.9) | 3 (100.0) | | | | |
| *S. pneumoniae* (1,878) | ≤0.015 | ≤0.015 | **1,867 (99.4)** | 11 (100.0) | – | – | – | – | – | – | – |
| VGS (522) | ≤0.015 | 0.03 | **332 (63.6)** | 178 (97.7) | 12 (100.0) | – | – | – | – | – | – |
| *S. anginosus* group (176) | ≤0.015 | 0.03 | **111 (63.1)** | 62 (98.3) | 3 (100.0) | – | – | – | – | – | – |
| BHS (1057) | ≤0.015 | 0.03 | **684 (64.7)** | 333 (96.2) | 36 (99.6) | 4 (100.0) | – | – | – | – | – |
| *S. pyogenes* (478) | ≤0.015 | 0.03 | **416 (87.0)** | 41 (95.6) | 20 (99.8) | 1 (100.0) | – | – | – | – | – |
| *S. agalactiae* (438) | 0.03 | 0.03 | 139 (31.7) | **283 (96.3)** | 13 (99.3) | 3 (100.0) | – | – | – | – | – |
| *S. dysgalactiae* (140) | ≤0.015 | ≤0.015 | **128 (91.4)** | 9 (97.9) | 3 (100.0) | – | – | – | – | – | – |

BMD = broth microdilution; MIC = minimum inhibitory concentration.
[a] BHS = β-hemolytic streptococci; CoNS = coagulase-negative staphylococci; MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-susceptible *S. aureus*; VanA = vancomycin and teicoplanin MIC values of >4 and >8 µg/mL, respectively; VanB = vancomycin and teicoplanin MIC values of >4 and ≤8 µg/mL, respectively; VGS = viridans group streptococci.
[b] Modal MIC values are shown in bold.
[c] All VanA phenotype.

### Antimicrobial susceptibility test methods

- Isolates were tested for susceptibility by broth microdilution following the CLSI guidelines (M07-A9).[6] Telavancin susceptibility was determined using the revised testing method following the CLSI (M100-S24)[1] and product package insert information.[2]
- MIC values were quality assured by concurrent testing of CLSI-recommended quality control (QC) reference strains (*S. aureus* American Type Culture Collection [ATCC] 29213, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619).[1] Telavancin MIC ranges, when tested against ATCC strains, were those for the revised method recently approved by the FDA and CLSI.[1,2,7] All QC results were within published acceptable CLSI ranges. Bacterial inoculum density was monitored by colony counts to assure an adequate number of cells for each testing event.
- MIC interpretations for telavancin were based on recently approved breakpoint criteria appropriate for the revised broth microdilution testing method, as specified in the updated product package insert,[2] and are as follows: *S. aureus* at ≤0.12 µg/mL for susceptible; *E. faecalis* (vancomycin-susceptible) at ≤0.25 µg/mL for susceptible; *Streptococcus pyogenes* and *Streptococcus agalactiae* at ≤0.12 µg/mL for susceptible; and *Streptococcus anginosus* group at ≤0.06 µg/mL for susceptible. The CLSI M100-S24[1] and European Committee on Antimicrobial Susceptibility Testing[8] breakpoint criteria were applied for comparator agents, as available.

## RESULTS

- Overall, telavancin had $MIC_{50}$ and $MIC_{90}$ values of 0.03 and 0.06 µg/mL against staphylococci, respectively, regardless of methicillin susceptibility, and inhibited all *S. aureus* at the revised FDA breakpoint for susceptibility (≤0.12 µg/mL; **Table 1**).
- *S. aureus* collected from North America, Europe, and Latin America showed telavancin $MIC_{50}$ values of 0.03 µg/mL (59.5–81.1% of isolates inhibited at 0.03 µg/mL), while isolates from the APAC region displayed a $MIC_{50}$ value of 0.06 µg/mL (41.1% of isolates inhibited at 0.03 µg/mL; data not shown).
- Telavancin also exhibited similar activity ($MIC_{50/90}$, 0.03/0.06 µg/mL) against North American (81.2% inhibited at ≤0.03 µg/mL) and European (76.0% inhibited at ≤0.03 µg/mL) MRSA strains, whereas slightly higher $MIC_{50}$ values ($MIC_{50/90}$, 0.06/0.06 µg/mL) were noted against those from Latin America (40.9% inhibited at ≤0.03 µg/mL) and APAC (32.7% inhibited at ≤0.03 µg/mL; data not shown).
- Overall, telavancin ($MIC_{50/90}$, 0.03/0.06 µg/mL) was 8-fold more potent than daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL) and 16- to 32-fold more active than vancomycin ($MIC_{50/90}$, 1/1 µg/mL) and linezolid ($MIC_{50/90}$, 1/1 µg/mL) against all *S. aureus* (**Table 2**).
- Telavancin exhibited overall $MIC_{50}$ and $MIC_{90}$ results of 0.03 and 0.06 µg/mL, respectively, when tested against the collection of coagulase-negative staphylococci (CoNS); these results were equivalent to those observed against methicillin-susceptible and -resistant CoNS, or isolates from various geographic regions (**Table 1** and **Table 2**).
- Telavancin ($MIC_{50/90}$, 0.03/0.06 µg/mL) was 8- to 16-fold more potent than daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL) and linezolid ($MIC_{50/90}$, 0.5/1 µg/mL), and 32-fold more active than vancomycin ($MIC_{50/90}$, 1/2 µg/mL) against the entire population of CoNS (**Table 2**).
- Telavancin ($MIC_{50/90}$, 0.12/0.12 µg/mL) was potent *in vitro* when tested against *E. faecalis*, inhibiting 98.4% of all strains or >99.9% of vancomycin-susceptible isolates at the FDA breakpoint for susceptibility (ie, ≤0.25 µg/mL; **Table 1**). All isolates displaying telavancin MIC values of ≥2 µg/mL had a VanA resistance phenotype.
- Based on $MIC_{50}$ values, telavancin ($MIC_{50/90}$, 0.12/0.12 µg/mL) was 8- to 16-fold more potent than vancomycin ($MIC_{50/90}$, 1/2 µg/mL), daptomycin ($MIC_{50/90}$, 1/1 µg/mL), linezolid ($MIC_{50/90}$, 1/1 µg/mL), and ampicillin ($MIC_{50/90}$, 1/2 µg/mL) when tested against vancomycin-susceptible *E. faecalis* (**Table 2**).
- Vancomycin-susceptible ($MIC_{50/90}$, ≤0.015/0.03 µg/mL) and -resistant (VanB; $MIC_{50/90}$, ≤0.015/0.25 µg/mL) *E. faecium* displayed low MIC values for telavancin (**Table 1**). Isolates displaying a VanA phenotype had higher telavancin MIC results ($MIC_{50/90}$, 1/2 µg/mL; lowest MIC at 0.25 µg/mL).
- Streptococci exhibited very low MIC results for telavancin ($MIC_{50}$, ≤0.015/0.3 µg/mL), which inhibited all isolates at ≤0.12 µg/mL (**Table 1**). In addition, telavancin showed the lowest MIC results against *S. pneumoniae* and viridans group streptococci (VGS) among tested agents, while telavancin and penicillin were the most active against β-hemolytic streptococci (BHS; **Table 2**).

## CONCLUSIONS

- Overall, telavancin showed very potent *in vitro* activity against *S. aureus* ($MIC_{50/90}$, 0.03/0.06 µg/mL), regardless of methicillin susceptibility patterns, as well as against CoNS ($MIC_{50/90}$, 0.03/0.06 µg/mL).
- Telavancin showed good activity when tested against vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.12/0.12 µg/mL) and *E. faecium* ($MIC_{50/90}$, ≤0.015/0.03 µg/mL) clinical isolates. *E. faecalis* and *E. faecium* isolates displaying a VanA phenotype had higher telavancin MIC results (≥2 and ≥0.25 µg/mL, respectively).
- Potent activity was observed when telavancin was tested against *S. pneumoniae* ($MIC_{90}$, ≤0.015 µg/mL), VGS ($MIC_{50}$, 0.03 µg/mL), and BHS ($MIC_{50}$, 0.03 µg/mL) clinical isolates, inhibiting all isolates at ≤0.03, ≤0.06, and ≤0.12 µg/mL, respectively.
- Overall, telavancin demonstrated potent *in vitro* activity, which was often greater than comparator agents when tested against this large and contemporary (2013) collection of clinical pathogens.

## REFERENCES

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**Table 2. Antimicrobial activity of telavancin and comparator agents when tested against contemporary (2013) worldwide collection of clinical isolates using a recently approved revised BMD susceptibility testing method**

| | | MIC (µg/mL) | | % Susceptible/% intermediate/% resistant[a] | | |
|---|---|---|---|---|---|---|
| **Organism[a] (no. tested) antimicrobial agent** | **Range** | **50%** | **90%** | **CLSI** | **FDA** | **EUCAST** |
| MRSA (2,613) | | | | | | |
| Telavancin | ≤0.015 to 0.12 | 0.03 | 0.06 | –[b] / – / – | 100.0 / - / - | 100.0 / - / - |
| Vancomycin | 0.25 to 2 | 1 | 1 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Daptomycin | ≤0.06 to 1 | 0.25 | 0.5 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Linezolid | ≤0.12 to >8 | 1 | 1 | 99.9 / 0.0 / 0.1 | | 99.9 / 0.0 / 0.1 |
| Levofloxacin | ≤0.12 to >4 | 4 | >4 | 28.2 / 1.3 / 70.5 | | 28.2 / 1.3 / 70.5 |
| Erythromycin | ≤0.12 to >16 | >16 | >16 | 17.6 / 2.5 / 79.9 | | 17.8 / 0.7 / 81.5 |
| Clindamycin | ≤0.25 to >2 | ≤0.25 | >2 | 66.6 / 0.1 / 33.3 | | 66.3 / 0.3 / 33.4 |
| Gentamicin | ≤1 to >8 | ≤1 | >8 | 88.9 / 0.3 / 10.8 | | 88.2 / 0.0 / 11.8 |
| Tetracycline | 0.06 to >32 | 0.12 | 2 | 90.9 / 0.4 / 8.7 | | 89.6 / 0.9 / 9.5 |
| Trimethoprim-sulfamethoxazole | ≤0.5 to >4 | ≤0.5 | ≤0.5 | 97.4 / 0.0 / 2.6 | | 97.4 / 0.1 / 2.5 |
| CoNS (875) | | | | | | |
| Telavancin | ≤0.015 to 0.25 | 0.03 | 0.06 | – / – / – | – / – / – | – / – / – |
| Oxacillin | ≤0.25 to >2 | >2 | >2 | 21.7 / 0.0 / 78.3 | | 21.7 / 0.0 / 78.3 |
| Vancomycin | ≤0.12 to 2 | 1 | 2 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Daptomycin | ≤0.06 to 4 | 0.25 | 0.5 | 99.8 / – / – | | 99.8 / 0.0 / 0.2 |
| Linezolid | 0.25 to >8 | 0.5 | 1 | 99.7 / 0.0 / 0.3 | | 99.7 / 0.0 / 0.3 |
| Levofloxacin | ≤0.12 to >4 | 0.5 | >4 | 52.8 / 2.4 / 44.8 | | 52.8 / 2.4 / 44.8 |
| Erythromycin | ≤0.12 to >16 | >16 | >16 | 35.9 / 0.9 / 63.2 | | 35.9 / 0.6 / 63.5 |
| Clindamycin | ≤0.25 to >2 | ≤0.25 | >2 | 66.5 / 1.2 / 32.3 | | 65.7 / 0.8 / 33.5 |
| Gentamicin | ≤1 to >8 | ≤1 | >8 | 61.8 / 6.7 / 31.5 | | 57.9 / 0.0 / 42.1 |
| Tetracycline | ≤0.03 to >32 | 0.5 | 32 | 85.0 / 1.5 / 13.5 | | 80.8 / 3.2 / 16.0 |
| Trimethoprim-sulfamethoxazole | ≤0.5 to >4 | ≤0.5 | >4 | 63.7 / 0.0 / 36.3 | | 63.7 / 18.0 / 18.3 |
| *E. faecalis* (702) | | | | | | |
| Telavancin | ≤0.015 to >2 | 0.12 | 0.12 | – / – / – | 98.4[c] / – / – | – / – / – |
| Ampicillin | ≤0.25 to 4 | 1 | 2 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Vancomycin | 0.5 to >16 | 1 | 2 | 98.4 / 0.2 / 1.4 | | 98.4 / 0.0 / 1.6 |
| Daptomycin | ≤0.06 to 4 | 1 | 1 | 100.0 / – / – | | 100.0 / – / – |
| Linezolid | 0.25 to 2 | 1 | 1 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Levofloxacin | 0.25 to >4 | 1 | >4 | 73.5 / 0.6 / 25.9 | | 74.1 / 0.0 / 25.9 |
| Tetracycline | 0.06 to >32 | >32 | >32 | 21.5 / 0.8 / 77.7 | | – / – / – |
| Vancomycin-susceptible *E. faecium* (228) | | | | | | |
| Telavancin | ≤0.015 to 0.12 | ≤0.015 | 0.03 | – / – / – | – / – / – | – / – / – |
| Ampicillin | ≤0.25 to >8 | >8 | >8 | 11.0 / 0.0 / 89.0 | | 9.6 / 1.4 / 89.0 |
| Vancomycin | 0.5 to 4 | 1 | 1 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Daptomycin | ≤0.06 to 4 | 2 | 2 | 100.0 / – / – | | – / – / – |
| Linezolid | 0.5 to 2 | 1 | 1 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Levofloxacin | 1 to >4 | >4 | >4 | 10.5 / 4.0 / 85.5 | | 14.5 / 0.0 / 85.5 |
| Tetracycline | 0.12 to >32 | 0.5 | >32 | 52.9 / 0.8 / 46.3 | | – / – / – |
| *S. pneumoniae* (1,878) | | | | | | |
| Telavancin | ≤0.015 to 0.03 | ≤0.015 | ≤0.015 | – / – / – | – / – / – | – / – / – |
| Penicillin | ≤0.06 to 8 | ≤0.06 | 2 | 90.9 / 8.2 / 0.9[d] | | – / – / – |
| Penicillin | ≤0.06 to 8 | ≤0.06 | 2 | 60.5 / 21.0 / 18.5[e] | | 60.5 / 30.4 / 9.1 |
| Vancomycin | ≤0.12 to 0.5 | 0.25 | 0.5 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Linezolid | ≤0.06 to 1 | 0.12 | 0.25 | – / – / – | | – / – / – |
| Levofloxacin | ≤0.12 to 2 | 1 | 1 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Erythromycin | 0.25 to >4 | 1 | 1 | 98.9 / 0.2 / 0.9 | | 98.9 / 0.0 / 1.1 |
| Clindamycin | ≤0.12 to >16 | ≤0.12 | >16 | 57.8 / 0.8 / 41.4 | | 57.8 / 0.8 / 41.4 |
| Tetracycline | ≤0.25 to >2 | ≤0.25 | >2 | 75.3 / 0.4 / 24.3 | | 75.7 / 0.0 / 24.3 |
| VGS (522) | | | | | | |
| Telavancin | ≤0.015 to 0.06 | ≤0.015 | 0.03 | – / – / – | 100.0 / – / – | – / – / – |
| Penicillin | ≤0.06 to >8 | ≤0.06 | 0.5 | 77.0 / 19.7 / 3.3 | | 84.9 / 11.8 / 3.3 |
| Vancomycin | ≤0.12 to 1 | 0.5 | 1 | 100.0 / 0.0 / 0.0 | | 100.0 / 0.0 / 0.0 |
| Daptomycin | ≤0.06 to 2 | 0.25 | 1 | 99.2 / – / – | | – / – / – |
| Linezolid | ≤0.12 to 4 | 0.5 | 1 | 99.8 / – / – | | – / – / – |
| Levofloxacin | 0.25 to >4 | 1 | 2 | 96.3 / 0.6 / 3.1 | | – / – / – |
| Erythromycin | ≤0.12 to >16 | ≤0.12 | 16 | 58.7 / 2.7 / 38.6 | | – / – / – |
| Clindamycin | ≤0.25 to >2 | ≤0.25 | >2 | 87.1 / 1.0 / 11.9 | | 88.1 / 0.0 / 11.9 |
| Tetracycline | ≤0.03 to >32 | 0.5 | >32 | 67.4 / 3.1 / 29.5 | | – / – / – |
| BHS (1,057) | | | | | | |
| Telavancin | ≤0.015 to 0.12 | ≤0.015 | 0.03 | – / – / – | 100.0 / – / – | – / – / – |
| Penicillin | ≤0.06 to 0.12 | ≤0.06 | ≤0.06 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Vancomycin | ≤0.12 to 0.5 | 0.25 | 0.5 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Daptomycin | ≤0.06 to 1 | ≤0.06 | 0.25 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Linezolid | ≤0.12 to 1 | 1 | 1 | 100.0 / – / – | | 100.0 / 0.0 / 0.0 |
| Levofloxacin | ≤0.12 to >4 | 0.5 | 1 | 99.3 / 0.2 / 0.5 | | 95.4 / 3.9 / 0.7 |
| Erythromycin | ≤0.12 to >16 | ≤0.12 | >16 | 72.6 / 1.1 / 26.3 | | 72.6 / 1.1 / 26.3 |
| Clindamycin | ≤0.25 to >2 | ≤0.25 | >2 | 85.7 / 0.4 / 13.9 | | 86.1 / 0.0 / 13.9 |
| Tetracycline | 0.06 to >32 | 1 | >32 | 51.3 / 1.9 / 46.8 | | 50.2 / 1.1 / 48.7 |

BMD = broth microdilution; CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FDA = U.S. Food and Drug Administration; MIC = minimum inhibitory concentration.
[a] BHS = β-hemolytic streptococci; CoNS = coagulase-negative staphylococci; MRSA = methicillin-resistant *S. aureus*; VGS = viridans group streptococci.
[b] Breakpoint criteria for telavancin according to the labeling supplement for the product (VIBATIV®), as available. *S. aureus* at ≤0.12 µg/mL for susceptible; *E. faecalis* (vancomycin-susceptible) at ≤0.25 µg/mL for susceptible. Breakpoint for VGS was that from *S. anginosus* group (≤0.06 µg/mL for susceptible); while the interpretive criterion for *S. pyogenes* and *S. agalactiae* (≤0.12 µg/mL for susceptible) was applied for BHS. Breakpoint criteria for comparator agents were those from CLSI (M100-S24, 2014) and EUCAST (2014), as available.
[c] Breakpoint not available.
[d] All vancomycin-susceptible *E. faecalis* were inhibited by the FDA-approved breakpoint for susceptibility (ie, ≤0.25 µg/mL), except for 1 isolate (MIC, 0.5 µg/mL).
[e] Susceptibility breakpoints for parenteral penicillin (non-meningitis).
[f] Susceptibility breakpoints for oral penicillin.

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