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Update on Telavancin Activity Tested Against a Collection of Gram-Positive Pathogens from US Hospitals (2007–2009)

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ABSTRACT

Background. Telavancin was approved (2009) in the US and Canada for the treatment of complicated skin and skin-structure infections (cSSSI). Telavancin is under review for complicated skin and soft-tissue infections in Europe and for nosocomial pneumonia in the US and Europe. Telavancin activity was assessed against Gram-positive isolates as part of a global surveillance study.

Methods. 14800 Gram-positive isolates were collected from 43 US sites. Identification was performed by standard algorithms and Vitek 2. Isolates were tested for susceptibility by CLSI methods (M07-A8 and M100-S20). Telavancin MIC results were interpreted based on approved US-FDA breakpoints, when available.

Results. Isolates were from bacteremia (44%), respiratory tract infections (19%), and cSSSI (18%). Telavancin (100% susceptible) was very potent against methicillin-resistant *S. aureus* (Table), for which only daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL; 99.8% susceptible) and quinupristin/dalfopristin ($MIC_{50/90}$, 0.5/0.5 µg/mL; 99.6% susceptible) exhibited similar activity. Telavancin (100% susceptible), daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL; 99.6% susceptible) and quinupristin/dalfopristin ($MIC_{50/90}$, ≤0.25/0.5 µg/mL; 99.7% susceptible) were the most active drugs against coagulase-negative staphylococci (73.3% methicillin-resistant). Telavancin inhibited 96.5% of *E. faecalis* at the US-FDA breakpoint (≤1 µg/mL), where ampicillin (99.9% susceptible), daptomycin (99.9% susceptible), and linezolid (100% susceptible) also showed good coverage. Telavancin inhibited, respectively, 100.0% and 91.7% of VanB-type *E. faecalis* and *E. faecium* at ≤1 µg/mL, whereas it was less active against VanA-type strains. Telavancin was uniformly active against *S. pneumoniae*, regardless of resistance to other drugs. Telavancin showed equivalent MIC_{50} values against resistant viridans group streptococci or β-hemolytic streptococci compared to susceptible strains.

Conclusions. This assessment reveals continued potent activity of telavancin against Gram-positive isolates from US hospitals and confirms the higher MIC values for VanA enterococci as noted earlier.

	MIC (µg/mL)		Number (cumulative %) inhibited at MIC (µg/mL)						
Organism (no. tested)	50%	90%	≤0.03	0.06	0.12	0.25	0.5	1	2
MSSA (3764)	0.12	0.25	19 (0.5)	264 (7.5)	2482 (73.5)	941 (98.5)	58 (100.0)	–	–
MRSA (4278)	0.12	0.25	4 (0.1)	139 (3.3)	2798 (68.8)	1240 (97.7)	97 (100.0)	–	–
CoNS (1240)	0.12	0.25	21 (1.7)	143 (13.2)	740 (72.9)	308 (97.7)	28 (100.0)	–	–
All *E. faecalis* (1442)	0.25	0.5	1 (0.07)	6 (0.5)	192 (13.8)	641 (58.2)	525 (94.7)	26 (96.5)	3 (96.7)[a]
VA-S *E. faecalis* (1376)	0.25	0.5	1 (0.1)	6 (0.5)	191 (14.4)	630 (60.2)	523 (98.2)	25 (100.0)	–
VanA-type *E. faecalis* (50)	>2	>2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (6.0)
VanB-type *E. faecalis* (15)	0.25	1	0 (0.0)	0 (0.0)	1 (6.7)	11 (80.0)	2 (93.3)	1 (100.0)	–
VA-S *E. faecium* (196)	0.12	0.25	26 (13.3)	50 (38.8)	88 (83.7)	30 (99.0)	1 (99.5)	1 (100.0)	–
VanA-type *E. faecium* (646)	2	>2	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	7 (1.2)	45 (8.2)	280 (51.6)
VanB-type *E. faecium* (24)	0.12	1	2 (8.3)	4 (25.0)	9 (62.5)	4 (79.2)	1 (83.3)	2 (91.7)	1 (100.0)
Pen-S SPN (1176)	≤0.03	≤0.03	1143 (97.2)	32 (99.9)	1 (100.0)	–	–	–	–
Pen-non-S SPN (210)	≤0.03	≤0.03	203 (96.7)	7 (100.0)	–	–	–	–	–
Pen- and Ery-non-S SPN (609)	≤0.03	≤0.03	594 (97.5)	15 (100.0)	–	–	–	–	–
Pen-S VGS (248)	≤0.03	0.06	129 (52.0)	104 (94.0)	14 (99.6)	1 (100.0)	–	–	–
Pen- and Ery-non-S VGS (75)	0.06	0.06	35 (46.7)	37 (96.0)	3 (100.0)	–	–	–	–
Ery-S BHS (623)	0.06	0.06	293 (47.0)	274 (91.0)	55 (99.8)	1 (100.0)	–	–	–
Ery-non-S BHS (256)	0.06	0.12	47 (18.4)	160 (80.9)	47 (99.2)	2 (100.0)	–	–	–

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VA-S, vancomycin-susceptible; Pen-S SPN, penicillin-susceptible *S. pneumoniae*; Pen-non-S SPN, penicillin-non-susceptible *S. pneumoniae*; Pen- and Ery-non-S SPN, penicillin- and erythromycin-non-susceptible *S. pneumoniae*; Pen-S VGS, penicillin-susceptible viridans group streptococci; Pen- and Ery-non-S VGS, penicillin- and erythromycin-non-susceptible viridans group streptococci; Ery-S BHS, erythromycin-susceptible β-hemolytic streptococci; Ery-non-S BHS, erythromycin-non-susceptible β-hemolytic streptococci. [a]All VanA-type *E. faecalis*

INTRODUCTION

- Telavancin is a once-daily intravenous semi-synthetic lipoglycopeptide with demonstrated potent *in vitro* activity against Gram-positive clinical isolates.[1-3]
- The bactericidal activity of telavancin results from a dual mode of action that involves inhibition of bacterial cell wall peptidoglycan biosynthesis and disruption of bacterial cell membrane function.[4]
- In Phase 3 trials, telavancin (10 mg/kg IV every 24h) demonstrated non-inferiority to vancomycin (1 g IV every 12h; dose adjusted per site-specific practice) treatment for complicated skin and skin-structure infections (cSSSI) and nosocomial pneumonia (NP).[5-7]
- Telavancin is indicated in the US and Canada for the treatment of cSSSI caused by susceptible Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), in adult patients.[7] Telavancin is under review for complicated skin and soft-tissue infections in Europe and for nosocomial pneumonia in the US and Europe.
- The aim of this study was to provide an update on telavancin activity against Gram-positive isolates recovered from US hospitals as part of a global surveillance study (2007–2009).

MATERIALS AND METHODS

Bacterial strain collection

- A total of 14800 non-duplicate Gram-positive clinical isolates were collected from 43 medical sites in the US in a prevalence mode design.
- Isolates were from bacteremia (44%), respiratory tract infections (19%), and cSSSI (18%) and submitted to a monitoring laboratory (JMI Laboratories, North Liberty, Iowa, US).
- Species identifications were confirmed by the monitoring laboratory using standard algorithms and the automated Vitek 2 system (bioMérieux, Hazelwood, Missouri, US), when necessary.

Antimicrobial susceptibility test methods

- Isolates were tested for susceptibility by using the reference broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI; M07-A8, 2009) recommendations.[8]
- Susceptibility testing was performed using commercially prepared and validated panels (TREK Diagnostic Systems, Cleveland, Ohio, US) in cation-adjusted Mueller-Hinton broth (with 2–5% lysed horse blood added for testing of streptococci).
- Validation of the minimum inhibitory concentration (MIC) values was performed by concurrent testing of CLSI-recommended (M100-S20, 2010)[9] quality control (QC) strains: *Enterococcus faecalis* ATCC 29212, *S. aureus* ATCC 29213, and *Streptococcus pneumoniae* ATCC 49619.
- Interpretation of MIC results was in accordance with published CLSI (M100-S20) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint criteria.[9,10] Telavancin breakpoints for susceptibility for *S. aureus* (≤1 µg/mL), β-hemolytic streptococci (BHS; ≤0.12 µg/mL), viridans group streptococci (VGS; ≤0.12 µg/mL), and *E. faecalis* (≤1 µg/mL) were those approved by the US Food and Drug Administration (FDA).[7]

RESULTS

- Telavancin ($MIC_{50/90}$, 0.12/0.25 µg/mL; 100% susceptible) was very active against MRSA and inhibited all strains at ≤0.5 µg/mL (**Table 1**). Daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL; 99.8% susceptible) and quinupristin/dalfopristin ($MIC_{50/90}$, 0.5/0.5 µg/mL; 99.6% susceptible; **Table 2**) exhibited similar MIC_{90} values when compared to telavancin.
- Other comparators, such as vancomycin, teicoplanin, linezolid, gentamicin, tetracycline, and trimethoprim/sulfamethoxazole also showed antimicrobial coverage (≥93.8% susceptible) when tested against MRSA (**Table 2**).
- A total of 73.3% of CoNS were methicillin-resistant, against which telavancin ($MIC_{50/90}$, 0.12/0.25 µg/mL), daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL; 99.7% susceptible), quinupristin/dalfopristin ($MIC_{50/90}$, ≤0.25/0.5 µg/mL; 99.6% susceptible), and linezolid ($MIC_{50/90}$, 1/1 µg/mL; 97.8% susceptible; **Table 2**) demonstrated activity.
- Telavancin inhibited 96.5% of *E. faecalis* at the FDA breakpoint (≤1 µg/mL; **Table 1**). Ampicillin (99.9% susceptible), daptomycin (99.9% susceptible), vancomycin (95.4% susceptible), teicoplanin (96.5% susceptible), and linezolid (100% susceptible) also showed good coverage (**Table 2**).
- All VanB-type *E. faecalis* ($MIC_{50/90}$, 0.25/1 µg/mL) and 91.7% of VanB-type *E. faecium* ($MIC_{50/90}$, 0.12/1 µg/mL) were inhibited by telavancin at ≤1 µg/mL (**Table 1**). Higher telavancin MIC results were noted among VanA-type enterococci.
- Only daptomycin (99.5% susceptible), linezolid (98.2% susceptible), and quinupristin/dalfopristin (91.5% susceptible) demonstrated acceptable (≥90.0% susceptible) antimicrobial activity against the *E. faecium* isolates collected (**Table 2**).
- Telavancin ($MIC_{50/90}$, ≤0.03/≤0.03 µg/mL) exhibited pronounced activity when tested against *S. pneumoniae*, regardless of penicillin or erythromycin resistance phenotypes (**Table 1**). In addition, telavancin MIC_{90} values (0.03 µg/mL) were 8- to 32-fold lower than daptomycin ($MIC_{50/90}$, 0.12/0.25 µg/mL), quinupristin/dalfopristin ($MIC_{50/90}$, 0.5/0.5 µg/mL), vancomycin ($MIC_{50/90}$, 1/1 µg/mL), linezolid ($MIC_{50/90}$, 1/1 µg/mL), and levofloxacin ($MIC_{50/90}$, 1/1 µg/mL) when tested against all *S. pneumoniae*.
- While equivalent telavancin MIC_{50} results (MIC_{50}, ≤0.06 µg/mL) were noted against VGS and BHS, a slightly higher (2-fold) MIC_{90} value (MIC_{90}, 0.12 µg/mL) was observed against erythromycin-non-susceptible BHS (**Table 1**).

CONCLUSIONS

- Telavancin ($MIC_{50/90}$, 0.12/0.25 µg/mL) demonstrated potent activity when tested against staphylococci and inhibited all isolates from the US at ≤0.5 µg/mL.
- Except for one *E. faecium*, all vancomycin-susceptible and VanB-type enterococci were inhibited by telavancin at ≤1 µg/mL. In contrast, telavancin was less active against VanA-type strains as previously reported.[1-3]
- Telavancin was very potent against *S. pneumoniae*, VGS, and BHS with MIC_{90} results of 0.03, 0.06, and 0.12 µg/mL, respectively. In addition, telavancin activity was not adversely affected when tested against isolates exhibiting various resistance phenotypes.
- This assessment reveals potent activity of telavancin against contemporary Gram-positive isolates from US hospitals.

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Table 1. Antimicrobial activity of telavancin tested against Gram-positive pathogens recovered from the US (2007–2009)

	MIC (µg/mL)		Number (cumulative %) inhibited at MIC (µg/mL)						
Organism (number tested)	50%	90%	≤0.03	0.06	0.12	0.25	0.5	1	2
MSSA (3764)	0.12	0.25	19 (0.5)	264 (7.5)	2482 (73.5)	941 (98.5)	58 (100.0)	–	–
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CoNS (1240)	0.12	0.25	21 (1.7)	143 (13.2)	740 (72.9)	308 (97.7)	28 (100.0)	–	–
All *E. faecalis* (1442)	0.25	0.5	1 (0.07)	6 (0.5)	192 (13.8)	641 (58.2)	525 (94.7)	26 (96.5)	3 (96.7)[a]
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VanA-type *E. faecalis* (50)	>2	>2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (6.0)
VanB-type *E. faecalis* (15)	0.25	1	0 (0.0)	0 (0.0)	1 (6.7)	11 (80.0)	2 (93.3)	1 (100.0)	–
VA-S *E. faecium* (196)	0.12	0.25	26 (13.3)	50 (38.8)	88 (83.7)	30 (99.0)	1 (99.5)	1 (100.0)	–
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Pen-S SPN (1176)	≤0.03	≤0.03	1143 (97.2)	32 (99.9)	1 (100.0)	–	–	–	–
Pen-non-S SPN (210)	≤0.03	≤0.03	203 (96.7)	7 (100.0)	–	–	–	–	–
Pen- and Ery-non-S SPN (609)	≤0.03	≤0.03	594 (97.5)	15 (100.0)	–	–	–	–	–
Pen-S VGS (248)	≤0.03	0.06	129 (52.0)	104 (94.0)	14 (99.6)	1 (100.0)	–	–	–
Pen- and Ery-non-S VGS (75)	0.06	0.06	35 (46.7)	37 (96.0)	3 (100.0)	–	–	–	–
Ery-S BHS (623)	0.06	0.06	293 (47.0)	274 (91.0)	55 (99.8)	1 (100.0)	–	–	–
Ery-non-S BHS (256)	0.06	0.12	47 (18.4)	160 (80.9)	47 (99.2)	2 (100.0)	–	–	–

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VA-S, vancomycin-susceptible; Pen-S SPN, penicillin-susceptible *S. pneumoniae*; Pen-non-S SPN, penicillin-non-susceptible *S. pneumoniae*; Pen- and Ery-non-S SPN, penicillin- and erythromycin-non-susceptible *S. pneumoniae*; Pen-S VGS, penicillin-susceptible viridans group streptococci; Pen- and Ery-non-S VGS, penicillin- and erythromycin-non-susceptible viridans group streptococci; Ery-S BHS, erythromycin-susceptible β-hemolytic streptococci; Ery-non-S BHS, erythromycin-non-susceptible β-hemolytic streptococci. [a]All VanA-type *E. faecalis*

Table 2. Antimicrobial activity of telavancin and comparator antimicrobial agents against Gram-positive pathogens recovered from the US (2007–2009)

Organism (number tested)	MIC (µg/mL)			% Susceptible/Resistant[a]	
Antimicrobial agent	Range	50%	90%	CLSI	EUCAST
MRSA (4278)					
Telavancin	≤0.015–0.5	0.12	0.25	100.0[b] / - [c]	
Vancomycin	0.25–4	1	1	>99.9 / 0.0	>99.9 / <0.1
Teicoplanin	≤2–8	≤2	≤2	100.0 / 0.0	99.6 / 0.4
Daptomycin	≤0.06–4	0.25	0.5	99.8 / -	99.8 / 0.2
Linezolid	0.25–>8	2	2	99.9 / 0.1	99.9 / 0.1
Quinupristin/dalfopristin	≤0.25–>2	0.5	0.5	99.6 / <0.1	99.6 / <0.1
Levofloxacin	≤0.5–>4	>4	>4	28.0 / 71.3	28.0 / 71.3
Erythromycin	≤0.25–>2	>2	>2	7.1 / 92.6	7.2 / 92.6
Clindamycin	≤0.25–>2	≤0.25	>2	64.5 / 35.2	64.2 / 35.5
Gentamicin	≤2–>8	≤2	≤2	97.2 / 2.6	96.9 / 3.1
Tetracycline	≤2–>8	≤2	≤2	94.7 / 5.0	93.8 / 6.2
Trimethoprim/sulfamethoxazole	≤0.5–>2	≤0.5	≤0.5	98.2 / 1.8	98.2 / 1.8
MRCoNS (909)					
Telavancin	≤0.015–0.5	0.12	0.25	- / -	- / -
Vancomycin	0.25–8	2	2	99.9 / 0.0	99.3 / 0.7
Teicoplanin	≤2–>16	≤2	8	94.9 / 0.6	86.5 / 13.5
Daptomycin	≤0.06–4	0.25	0.5	99.7 / -	99.7 / 0.3
Linezolid	0.25–>8	1	1	97.8 / 2.2	97.8 / 2.2
Quinupristin/dalfopristin	≤0.25–2	≤0.25	0.5	99.6 / 0.0	99.6 / 0.0
Levofloxacin	≤0.5–>4	>4	>4	27.8 / 69.9	27.8 / 69.9
Erythromycin	≤0.25–>2	>2	>2	22.0 / 77.1	22.2 / 77.1
Clindamycin	≤0.25–>2	≤0.25	>2	53.5 / 44.6	52.7 / 46.5
Gentamicin	≤2–>8	≤2	>8	58.6 / 28.5	53.0 / 47.0
Tetracycline	≤2–>8	≤2	>8	87.0 / 12.3	85.3 / 14.7
Trimethoprim/sulfamethoxazole	≤0.5–>2	2	>2	54.7 / 45.3	54.7 / 45.3
E. faecalis (1442)					
Telavancin	0.03–>2	0.25	0.5	96.5[b] / -	
Ampicillin	≤1–>16	≤1	2	99.9 / 0.1	99.9 / 0.1
Vancomycin	≤0.12–>16	1	2	95.4 / 4.4	95.4 / 4.6
Teicoplanin	≤2–>16	≤2	≤2	96.5 / 3.5	96.5 / 3.5
Daptomycin	≤0.06–8	1	2	99.9 / -	- / -
Linezolid	0.25–2	1	2	100.0 / 0.0	100.0 / 0.0
Quinupristin/dalfopristin	≤0.25–>2	>2	>2	0.5 / 96.5	0.5 / 96.5
Levofloxacin	≤0.5–>4	1	>4	67.1 / 32.5	- / -
E. faecium (866)					
Telavancin	≤0.015–>2	2	>2	- / -	- / -
Ampicillin	≤1–>16	>16	>16	5.8 / 94.2	5.7 / 94.2
Vancomycin	0.25–>16	>16	>16	22.6 / 76.9	22.6 / 77.4
Teicoplanin	≤2–>16	>16	>16	25.3 / 69.5	24.5 / 75.5
Daptomycin	≤0.06–>8	2	2	99.5 / -	- / -

Organism (number tested)	MIC (µg/mL)			% Susceptible/Resistant[a]	
Antimicrobial agent	Range	50%	90%	CLSI	EUCAST
E. faecium (cont)					
Linezolid	0.5–>8	1	2	98.2 / 1.8	98.2 / 1.8
Quinupristin/dalfopristin	≤0.25–>2	0.5	1	91.5 / 4.8	91.5 / 4.8
Levofloxacin	≤0.5–>4	>4	>4	5.0 / 93.3	- / -
Tetracycline	≤2–>8	≤2	>8	53.2 / 46.2	- / -
S. pneumoniae (1995)					
Telavancin	≤0.015–0.12	≤0.015	0.03	- / -	- / -
Penicillin[d]	≤0.03–>4	≤0.03	4	86.7 / 1.2	- / -
Penicillin[e]	≤0.03–>4	≤0.03	4	58.9 / 20.8	58.9 / 13.3
Vancomycin	≤1–1	1	1	100.0 / -	100.0 / 0.0
Teicoplanin	≤2	≤2	≤2	- / -	100.0 / 0.0
Daptomycin	≤0.06–1	0.12	0.25	- / -	- / -
Linezolid	≤0.12–2	1	1	100.0 / -	100.0 / 0.0
Quinupristin/dalfopristin	≤0.25–2	0.5	0.5	99.8 / 0.0	- / -
Levofloxacin	≤0.5–>4	1	1	99.3 / 0.6	99.3 / 0.7
Erythromycin	≤0.25–>2	≤0.25	>2	61.3 / 38.2	61.3 / 38.2
Clindamycin	≤0.25–>2	≤0.25	>2	80.0 / 19.6	80.4 / 19.6
Tetracycline	≤2–>8	≤2	>8	76.0 / 23.5	76.0 / 24.0
Viridans group streptococci (336)[f]					
Telavancin	≤0.015–0.25	0.03	0.06	100.0[b] / -	
Penicillin	≤0.015–32	0.06	1	73.8 / 5.4	81.3 / 5.4
Vancomycin	≤0.12–1	0.5	1	100.0 / -	100.0 / 0.0
Teicoplanin	≤2–4	≤2	≤2	- / -	99.1 / 0.9
Daptomycin	≤0.06–2	0.25	1	99.4 / -	- / -
Linezolid	0.12–2	1	1	100.0 / -	- / -
Quinupristin/dalfopristin	≤0.25–>2	0.5	1	97.6 / 0.3	- / -
Levofloxacin	≤0.5–>4	1	2	90.5 / 8.0	- / -
Erythromycin	≤0.25–>2	1	>2	42.9 / 53.9	- / -
Clindamycin	≤0.25–>2	≤0.25	0.5	89.9 / 8.3	91.7 / 8.3
Tetracycline	≤2–>8	≤2	>8	68.2 / 27.1	- / -
β-hemolytic streptococci (879)[g]					
Telavancin	≤0.015–0.25	0.06	0.12	99.7[b] / -	
Penicillin	≤0.015–0.12	≤0.015	0.06	100.0 / -	100.0 / 0.0
Vancomycin	≤0.12–1	0.5	0.5	100.0 / -	100.0 / 0.0
Teicoplanin	≤2–4	≤2	≤2	- / -	99.9 / 0.1
Daptomycin	≤0.06–0.5	0.12	0.25	100.0 / -	100.0 / 0.0
Linezolid	≤0.06–2	1	1	100.0 / -	100.0 / 0.0
Quinupristin/dalfopristin	≤0.25–1	≤0.25	0.5	100.0 / 0.0	- / -
Levofloxacin	≤0.5–>4	≤0.5	1	98.7 / 1.0	95.3 / 1.3
Erythromycin	≤0.25–>2	≤0.25	>2	70.9 / 27.9	70.9 / 27.9
Clindamycin	≤0.25–>2	≤0.25	>2	86.2 / 13.5	86.5 / 13.5
Tetracycline	≤2–>8	4	>8	48.5 / 49.0	48.5 / 51.5

MIC, minimum inhibitory concentration; MRSA, methicillin-resistant *S. aureus*; MRCoNS, methicillin-resistant coagulase-negative staphylococci.
[a]Criteria for susceptibility as published by the Clinical and Laboratory Standards Institute (M100-S20, 2010) and European Committee on Antimicrobial Susceptibility Testing (2010).
[b]For telavancin, the US FDA approved breakpoints for susceptibility for *S. aureus* (≤1 µg/mL), viridans group streptococci (≤0.12 µg/mL), β-hemolytic streptococci (≤0.12 µg/mL), and vancomycin-susceptible *E. faecalis* (≤1 µg/mL) were applied.
[c]- indicates no breakpoint available.
[d]Penicillin parenteral (non-meningitis).
[e]Penicillin (oral penicillin V).
[f]Includes *S. anginosus* (27 strains), *S. constellatus* (12 strains), *S. gordonii* (2 strains), *S. intermedius* (4 strains), *S. milleri* (5 strains), *S. mitis* (74 strains), *S. mutans* (1 strain), *S. oralis* (8 strains), *S. parasanguinis* (16 strains), *S. salivarius* (15 strains), *S. sanguinis* (9 strains), *S. thermophilus* (1 strain), *S. uberis* (1 strain), *S. vestibularis* (2 strains), unspeciated alpha-hemolytic streptococci (6 strains), and unspeciated viridans group streptococci (153 strains).
[g]Includes *S. dysgalactiae* (8 strains), *S. equi* (1 strain), Group A streptococci (356 strains), Group B streptococci (410 strains), Group C streptococci (27 strains), Group F streptococci (8 strains), Group G streptococci (65 strains), and unspeciated β-hemolytic streptococci (4 strains).

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