Update on Telavancin Activity Tested Against a Global Collection of Gram-positive Pathogens (2010)

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ABSTRACT (REVISED)

Background. Telavancin is a lipoglycopeptide approved in the USA and Canada for the treatment of complicated skin and skin structure infections (cSSSI) caused by susceptible Gram-positive bacteria. Telavancin is under review for nosocomial pneumonia in the USA and Europe. This study provides an updated evaluation of telavancin activity against Gram-positive isolates from a global surveillance program.

Methods. 15,480 Gram-positive isolates were collected from 89 sites in the USA, Europe, Asia-Pacific, and Latin America in 2010. Identification was performed by standard algorithms and Vitek 2. Isolates were tested for susceptibility by CLSI methods (M07-A8 and M100-S21). Telavancin MIC results were interpreted using FDA breakpoints, as available.

Results. Telavancin (100% susceptible) was very active against MRSA (Table). Telavancin was 2-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL) and 4- to 8-fold more potent than vancomycin ($MIC_{50/90}$, 1/1 μg/mL) and linezolid ($MIC_{50/90}$, 1/1 μg/mL) against MRSA. Telavancin was 2-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL), and 8- to 16- fold more potent than vancomycin ($MIC_{50/90}$, 1/2 μg/mL) and teicoplanin ($MIC_{50/90}$, 2/4 μg/mL) against CoNS. *E. faecalis* were highly susceptible to telavancin (98% susceptible), except for VanA strains. Telavancin (MIC, ≤0.25 μg/mL) was active against vancomycin-susceptible *E. faecium*. Telavancin MIC_{50} results against *S. pneumoniae* were 8- to 32-fold lower than vancomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL; 100% susceptible), levofloxacin ($MIC_{50/90}$, 1/1 μg/mL; 99% susceptible) and linezolid ($MIC_{50/90}$, 1/1 μg/mL; >99% susceptible), and 128-fold lower than penicillin ($MIC_{50/90}$, ≤0.03/4 μg/mL; 88% susceptible (parenteral)). Telavancin and penicillin ($MIC_{50/90}$, ≤0.03/0.06 μg/mL) were similarly active against β-hemolytic streptococci and telavancin was ≥2-fold more potent than comparators against viridans group streptococci.

Conclusions. This study shows consistently potent telavancin activity against a contemporary, global collection of Gram-positive isolates. All clinically relevant pathogens were susceptible to telavancin (FDA breakpoints).

Organism (number tested)	MIC (μg/mL)		Number (cumulative %) inhibited at telavancin MIC (μg/mL) of:					
	50%	90%	≤0.03	0.06	0.12	0.25	0.5	1
MSSA (4,565)	0.12	0.25	7 (0.2)	172 (3.9)	2572 (60.3)	1660 (96.6)	154 (100.0)	–
MRSA (3,088)	0.12	0.25	1 (<0.1)	60 (2.0)	1583 (53.2)	1302 (95.4)	142 (100.0)	–
CoNS (1,278)	0.12	0.25	20 (1.6)	88 (8.5)	659 (60.0)	473 (97.0)	37 (99.9)	1 (100.0)
E. faecalis (1,459)	0.5	0.5	2 (0.1)	8 (0.7)	157 (11.4)	461 (43.0)	761 (95.2)	38 (97.8)
VA-S *E. faecium* (386)	0.06	0.12	91 (23.6)	114 (53.1)	152 (92.5)	29 (100.0)	–	–
SPN (2,150)	≤0.015	0.03	2140 (99.5)	8 (99.9)	2 (100.0)	–	–	–
BHS (1,472)	0.06	0.12	665 (45.2)	541 (81.9)	263 (99.8)	3 (100.0)	–	–
VGS (551)	0.03	0.06	411 (74.6)	112 (94.9)	28 (100.0)	–	–	–

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci; VA-S, vancomycin-susceptible; VGS, viridans group streptococci; BHS, β-hemolytic streptococci

INTRODUCTION

- Telavancin is a parenteral semi-synthetic lipoglycopeptide with concentration-dependent bactericidal activity due to a dual mechanism of action that combines inhibition of peptidoglycan synthesis and disruption of membrane potential and increased permeability.[1]
- Telavancin is approved in the USA and Canada for the treatment of adults with complicated skin and skin structure infections (cSSSI) caused by susceptible organisms.[2]
- This drug is also under review for the treatment of nosocomial pneumonia (NP) in the USA and Europe. In May 2011, the Committee for Medicinal Products for Human Use (CHMP) recommended the marketing authorization in Europe for the NP claim, including ventilator-associated pneumonia (VAP), that is known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA).
- The overall aim of this study was to provide an updated evaluation of the potency and spectrum of activity of telavancin against contemporary (2010) Gram-positive isolates from a global surveillance program.

MATERIALS AND METHODS

Bacterial strain collection

- A total of 15,480 Gram-positive clinical isolates were collected from 89 medical sites in the USA (26 hospitals; 6,719 isolates), Europe (31; 4,647), Latin America (10; 1,814), and the Asia-Pacific region (22; 2,300).
- Consecutive, non-duplicated clinical isolates were included. These strains were collected in a prevalence mode design from hospitalized patients following established protocols.
- Isolates were mostly recovered from bacteremia (39%), SSSI (28%), and respiratory tract infections (21%), and submitted to a monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) as part of the 2010 Telavancin Global Surveillance Program.
- Each primary medical center provided species identifications, which were confirmed by the monitoring laboratory using standard algorithms and the automated Vitek 2 system (bioMérieux, Hazelwood, Missouri, USA), when necessary.
- The distribution of leading species included were as follows: *S. aureus* (7,653; 49.4%), coagulase-negative staphylococci (CoNS; 1,278; 8.3%), *Enterococcus faecalis* (1,459; 9.4%), *Enterococcus faecium* (805; 5.2%), *Streptococcus pneumoniae* (2,150; 13.9%), β-hemolytic streptococci (BHS; 1,472; 9.5%), viridans group streptococci (VGS; 551; 3.6%), and *Streptococcus bovis* group (SBG; 32; 0.2%).

Antimicrobial susceptibility test methods

- Isolates were tested for susceptibility by the broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI; M07-A8, 2009) recommendations.[3]
- Susceptibility testing was performed using commercially prepared and validated panels (TREK Diagnostic Systems, Cleveland, Ohio, USA) 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-S21, 2011)[4] quality control (QC) strains: *E. faecalis* ATCC 29212, *S. aureus* ATCC 29213, and *S. pneumoniae* ATCC 49619.
- Interpretation of MIC results was in accordance with published CLSI (M100-S21) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint criteria.[4,5] Telavancin-susceptible breakpoints for *S. aureus* (≤1 μg/mL), vancomycin-susceptible *E. faecalis* (≤1 μg/mL), BHS (≤0.12 μg/mL), and VGS (≤0.12 μg/mL) were those approved by the US Food and Drug Administration (FDA).[2]
- Enterococcal isolates were clustered according to glycopeptide susceptibility. The VanA phenotype was characterized by non-susceptibility to vancomycin (≥8 μg/mL) and teicoplanin (≥16 μg/mL), while isolates with a VanB phenotype were those non-susceptible to vancomycin (≥8 μg/mL), but susceptible to teicoplanin (≤8 μg/mL), according to the CLSI interpretive criteria.[4]

RESULTS

- Resistance to oxacillin was observed in 40.4% and 74.0% of *S. aureus* and CoNS, respectively. Telavancin ($MIC_{50/90}$, 0.12/0.25 μg/mL) exhibited equivalent potencies when tested against *S. aureus* and CoNS and inhibited all isolates at ≤1 μg/mL, regardless of oxacillin resistance (**Table 1**).
- When tested against MRSA, telavancin ($MIC_{50/90}$, 0.12/0.25 μg/mL) was 2-fold more potent than daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL) and 4- to 8-fold more active than vancomycin ($MIC_{50/90}$, 1/1 μg/mL) and linezolid ($MIC_{50/90}$, 1/1 μg/mL; **Table 2**).
- When tested against a worldwide collection of CoNS, telavancin ($MIC_{50/90}$, 0.12/0.25 μg/mL) was 2-fold more potent than daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL) and 4- to 8-fold more active than linezolid ($MIC_{50/90}$, 0.5/1 μg/mL) and vancomycin ($MIC_{50/90}$, 1/2 μg/mL; **Table 2**).
- When tested against *E. faecalis*, telavancin ($MIC_{50/90}$, 0.5/0.5 μg/mL) inhibited 97.8% of clinical isolates at ≤1 μg/mL, including 6 VanB-type strains. All 32 *E. faecalis* exhibiting telavancin MIC at ≥2 μg/mL displayed a VanA phenotype (**Table 1**).
- When tested against all *E. faecalis*, telavancin ($MIC_{50/90}$, 0.5/0.5 μg/mL) demonstrated MIC_{50} values 2- to 4-fold lower than ampicillin ($MIC_{50/90}$, ≤1/2 μg/mL), vancomycin ($MIC_{50/90}$, 1/2 μg/mL), daptomycin ($MIC_{50/90}$, 1/1 μg/mL), and linezolid ($MIC_{50/90}$, 1/2 μg/mL; **Table 2**).
- Telavancin tested against vancomycin-susceptible *E. faecium* ($MIC_{50/90}$, 0.06/0.12 μg/mL) was 4- to 8-fold more active when compared with vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.5/0.5 μg/mL; **Table 1**).
- When tested against vancomycin-susceptible *E. faecium*, telavancin ($MIC_{50/90}$, 0.06/0.12 μg/mL) was 8- to 16-fold more active than vancomycin ($MIC_{50/90}$, 1/1 μg/mL) and 16- to 32-fold more active than daptomycin ($MIC_{50/90}$, 2/2 μg/mL; **Table 2**).
- VanB-type *E. faecium* ($MIC_{50/90}$, 0.12/0.5 μg/mL) exhibited higher telavancin MIC values when compared with vancomycin-susceptible strains ($MIC_{50/90}$, 0.06/0.12 μg/mL; **Table 1**), yet telavancin inhibited all strains at ≤1 μg/mL. VanA-type *E. faecium* showed decreased susceptibility to telavancin ($MIC_{50/90}$, 2/>2 μg/mL).
- Telavancin ($MIC_{50/90}$, ≤0.015/0.03 μg/mL) was very potent against *S. pneumoniae* isolates, from which 0.6% and 22.4% of *S. pneumoniae* were penicillin-resistant using the CLSI criteria (parenteral [≥8 μg/mL] and oral [≥2 μg/mL] therapy breakpoints, respectively; **Table 2**).
- Telavancin MIC_{50} results when tested against BHS serogroup B ($MIC_{50/90}$, 0.06/0.12 μg/mL) were slightly higher (2-fold) than those noted against serogroup A ($MIC_{50/90}$, 0.03/0.06 μg/mL), serogroup C ($MIC_{50/90}$, 0.03/0.06 μg/mL), serogroup F (MIC_{50}, 0.03 μg/mL), and serogroup G ($MIC_{50/90}$, 0.03/0.12 μg/mL; **Table 1**).
- Among VGS, 5.4% of strains were fully resistant to penicillin (**Table 2**). Telavancin ($MIC_{50/90}$, 0.03/0.06 μg/mL) was 2- to 16-fold more potent than penicillin ($MIC_{50/90}$, 0.06/1 μg/mL), daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL), vancomycin ($MIC_{50/90}$, 0.5/0.5 μg/mL), and linezolid ($MIC_{50/90}$, 1/1 μg/mL) when tested against VGS.

CONCLUSIONS

- Telavancin demonstrated potent in vitro activity when tested against a large collection of Gram-positive isolates recovered in 2010 from hospitalized patients on 4 continents.
- *S. aureus* and CoNS were inhibited by telavancin ($MIC_{50/90}$, 0.12/0.25 μg/mL) at the FDA susceptible breakpoint (≤1 μg/mL), as were all vancomycin-susceptible and VanB-type enterococci. VanA-type enterococci exhibited higher MIC values as previously documented.
- Telavancin was very potent against *S. pneumoniae*, VGS (99.7% susceptible), and BHS (99.8% susceptible) with MIC_{50} results of 0.03, 0.06, and 0.12 μg/mL, respectively. Moreover, SBG was very susceptible to telavancin ($MIC_{50/90}$, 0.06/0.06 μg/mL; 100.0% susceptible).
- In summary, telavancin continues to exhibit an overall in vitro activity similar or greater than that of comparator agents against indicated staphylococci, streptococci, and vancomycin-susceptible *E. faecalis* pathogens.

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Table 1. Antimicrobial activity of telavancin tested against a worldwide collection of Gram-positive clinical isolates (2010)

Organism/groups	MIC (μg/mL)		Number (cumulative %) of isolates inhibited at each telavancin MIC (μg/mL) of:							
Resistant subsets (numbered tested)	50%	90%	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2
Staphylococcus aureus (7653)	0.12	0.25	1 (0.0)	7 (0.1)	232 (3.1)	4155 (57.4)	2962 (96.1)	296 (100.0)	–	–
Oxacillin-susceptible (4565)	0.12	0.25	0 (0.0)	7 (0.2)	172 (3.9)	2572 (60.3)	1660 (96.6)	154 (100.0)	–	–
Oxacillin-resistant (3088)	0.12	0.25	1 (0.0)	0 (0.0)	60 (2.0)	1583 (53.2)	1302 (95.4)	142 (100.0)	–	–
CoNS (1278)	0.12	0.25	6 (0.5)	14 (1.6)	88 (8.5)	659 (60.0)	473 (97.0)	37 (99.9)	1 (100.0)	–
Oxacillin-susceptible (332)	0.12	0.25	0 (0.0)	9 (2.7)	36 (13.6)	166 (63.6)	115 (98.2)	6 (100.0)	–	–
Oxacillin-resistant (946)	0.12	0.25	6 (0.6)	5 (1.2)	52 (6.7)	493 (58.8)	358 (96.6)	31 (99.9)	1 (100.0)	–
Enterococcus faecalis (1459)	0.5	0.5	0 (0.0)	2 (0.1)	8 (0.7)	157 (11.4)	461 (43.0)	761 (95.2)	38 (97.8)	2 (97.9)
Vancomycin-susceptible (1421)	0.5	0.5	0 (0.0)	2 (0.1)	8 (0.7)	157 (11.8)	460 (44.1)	758 (97.5)	36 (100.0)	–
Vancomycin-non-susceptible[a] (38)	>2	>2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	3 (10.5)	2 (15.8)	2 (21.1)
Enterococcus faecium (805)	0.25	>2	10 (1.2)	86 (11.9)	117 (26.5)	164 (46.8)	33 (50.9)	11 (52.3)	33 (56.4)	156 (75.8)
Vancomycin-susceptible (386)	0.06	0.12	9 (2.3)	82 (23.6)	114 (53.1)	152 (92.5)	29 (100.0)	–	–	–
VanA-type *E. faecium* (392)	2	>2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	9 (2.6)	31 (10.5)	156 (50.3)
VanB-type *E. faecium* (27)	0.12	0.5	1 (3.7)	4 (18.5)	3 (29.6)	12 (74.1)	3 (85.2)	2 (92.6)	2 (100.0)	–
Streptococcus pneumoniae (2150)	≤0.015	0.03	1811 (84.2)	329 (99.5)	8 (99.9)	2 (100.0)	–	–	–	–
Penicillin-susceptible (1330)	≤0.015	0.03	1103 (82.9)	222 (99.6)	3 (99.8)	2 (100.0)	–	–	–	–
Penicillin-non-susceptible (820)	≤0.015	0.03	708 (86.3)	107 (99.4)	5 (100.0)	–	–	–	–	–
β-hemolytic streptococci (1472)	0.06	0.12	101 (6.9)	564 (45.2)	541 (81.9)	263 (99.8)	3 (100.0)	–	–	–
Group A Streptococcus (521)	0.03	0.06	95 (18.2)	346 (84.6)	60 (96.2)	20 (100.0)	–	–	–	–
Group B Streptococcus (669)	0.06	0.12	0 (0.0)	51 (7.6)	399 (67.3)	216 (99.6)	3 (100.0)	–	–	–
Group C Streptococcus (91)	0.03	0.06	2 (2.2)	54 (61.5)	27 (91.2)	8 (100.0)	–	–	–	–
Group F Streptococcus (8)	0.03	–	0 (0.0)	6 (75.0)	2 (100.0)	–	–	–	–	–
Group G Streptococcus (154)	0.03	0.12	3 (1.9)	87 (58.4)	47 (89.0)	17 (100.0)	–	–	–	–
Viridans group streptococci (551)	0.03	0.06	78 (14.2)	333 (74.6)	112 (94.9)	28 (100.0)	–	–	–	–
Streptococcus anginosus group (97)	0.03	0.06	7 (7.2)	68 (77.3)	19 (96.9)	3 (100.0)	–	–	–	–
Streptococcus bovis group (32)	0.03	0.06	4 (12.5)	19 (71.9)	6 (90.6)	3 (100.0)	–	–	–	–
Penicillin-susceptible (416)	0.03	0.06	66 (15.9)	254 (76.9)	80 (96.2)	16 (100.0)	–	–	–	–
Penicillin-non-susceptible (135)	0.03	0.06	12 (8.9)	79 (67.4)	32 (91.1)	12 (100.0)	–	–	–	–

MIC, minimum inhibitory concentration; CoNS, coagulase-negative staphylococci.
[a]Includes 32 and 6 VanA- and VanB-type strains, respectively.

Table 2. Antimicrobial activity of telavancin and comparator antimicrobial agents against a worldwide collection of Gram-positive clinical isolates (2010)

Organism (number tested)		MIC (μg/mL)		% Susceptible/Resistant[a]	
Antimicrobial agent	Range	50%	90%	CLSI	EUCAST
MSSA (4,565)					
Telavancin[b]	0.03 – 0.5	0.12	0.25	100.0 / –[c]	
Vancomycin	0.25 – 2	1	1	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤1 – 4	≤1	≤1	100.0 / 0.0	>99.9 / <0.1
Daptomycin	≤0.06 – 1	0.25	0.5	100.0 / –	100.0 / 0.0
Linezolid	≤0.12 – 2	1	2	100.0 / 0.0	100.0 / 0.0
Levofloxacin	≤0.5 – >4	≤0.5	≤0.5	91.7 / 7.6	91.7 / 7.6
Erythromycin	≤0.25 – >4	≤0.25	>4	76.4 / 21.7	76.4 / 22.7
Clindamycin	≤0.25 – >2	≤0.25	≤0.25	95.1 / 4.6	94.5 / 4.9
Tetracycline	≤0.25 – >8	≤0.25	0.5	94.3 / 5.0	93.6 / 6.1
Trimethoprim / sulfamethoxazole	≤0.5 – >4	≤0.5	≤0.5	99.1 / 0.9	99.1 / 0.7
MRSA (3,088)					
Telavancin	≤0.015 – 0.5	0.12	0.25	100.0 / –	
Vancomycin	0.25 – 2	1	1	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤1 – 4	≤1	≤1	100.0 / 0.0	99.5 / 0.5
Daptomycin	≤0.06 – 2	0.25	0.5	99.9 / –	99.9 / 0.1
Linezolid	≤0.12 – 8	1	1	>99.9 / <0.1	>99.9 / <0.1
Levofloxacin	≤0.5 – >4	>4	>4	24.1 / 74.1	24.1 / 74.1
Erythromycin	≤0.25 – >4	>4	>4	16.4 / 82.9	16.4 / 83.2
Clindamycin	≤0.25 – >2	≤0.25	>2	59.2 / 40.7	58.9 / 40.8
Tetracycline	≤0.25 – >8	≤0.25	>8	87.6 / 12.1	84.3 / 12.7
Trimethoprim / sulfamethoxazole	≤0.5 – >4	≤0.5	≤0.5	95.0 / 5.0	95.0 / 4.7
CoNS (1,278)					
Telavancin	≤0.015 – 1	0.12	0.25	– / –	– / –
Oxacillin	≤0.25 – >2	>2	>2	26.0 / 74.0	26.0 / 74.0
Vancomycin	0.25 – 4	1	2	100.0 / 0.0	99.3 / 0.7
Teicoplanin	≤1 – >8	2	4	99.1 / 0.0	90.8 / 9.2
Daptomycin	≤0.06 – 2	0.25	0.5	99.8 / –	99.8 / 0.2
Linezolid	≤0.12 – >8	0.5	1	99.4 / 0.6	99.4 / 0.6
Levofloxacin	≤0.5 – >4	2	>4	46.2 / 48.8	46.2 / 48.8
Erythromycin	≤0.25 – >4	>4	>4	36.1 / 62.6	36.1 / 63.2
Clindamycin	≤0.25 – >2	≤0.25	>2	65.5 / 33.0	64.2 / 34.5
Tetracycline	≤0.25 – >8	1	>8	85.2 / 13.4	72.0 / 16.1
Trimethoprim / sulfamethoxazole	≤0.5 – >4	≤0.5	>4	63.7 / 36.3	63.7 / 20.8
E. faecalis (1,459)[d]					
Telavancin	0.03 – >2	0.5	0.5	97.8 / –	
Ampicillin	≤1 – 8	≤1	2	100.0 / 0.0	99.6 / 0.0
Vancomycin	0.25 – >16	1	2	97.4 / 2.5	97.4 / 2.6
Teicoplanin	≤1 – >8	≤1	≤1	97.8 / 2.2	97.8 / 2.2
Daptomycin	≤0.06 – 4	1	1	100.0 / –	– / –
Linezolid	0.25 – >8	1	2	99.9 / 0.1	99.9 / 0.1
Levofloxacin	≤0.5 – >4	1	>4	67.6 / 31.9	– / –
E. faecium					
Vancomycin-susceptible (386)					
Telavancin	≤0.015 – 0.25	0.06	0.12	– / –	– / –
Ampicillin	≤1 – >8	>8	>8	14.2 / 85.8	13.7 / 85.8
Daptomycin	≤0.06 – 4	2	2	100.0 / –	– / –
Linezolid	0.5 – 8	1	2	99.2 / 0.8	99.2 / 0.8
Levofloxacin	≤0.5 – >4	>4	>4	12.7 / 82.9	– / –
Quinupristin / dalfopristin	≤0.5 – >4	≤0.5	4	71.8 / 11.9	71.8 / 1.0
VanA-type *E. faecium* (392)					
Telavancin	0.25 – >2	2	>2	– / –	– / –
Ampicillin	≤1 – >8	>8	>8	0.3 / 99.7	0.3 / 99.7
Daptomycin	0.12 – 8	2	2	99.5 / –	– / –
Linezolid	0.5 – >8	1	1	98.7 / 0.3	99.7 / 0.3
Levofloxacin	>4	>4	>4	0.0 / 100.0	– / –
Quinupristin / dalfopristin	≤0.5 – >4	≤0.5	1	97.2 / 1.0	97.2 / 1.0
VanB-type *E. faecium* (27)					
Telavancin	≤0.015 – 1	0.12	0.5	– / –	– / –
Ampicillin	>8	>8	>8	0.0 / 100.0	0.0 / 100.0
Daptomycin	0.12 – 2	2	2	100.0 / –	– / –
Linezolid	0.5 – 4	1	2	96.3 / 0.0	100.0 / 0.0
Levofloxacin	4 – >4	>4	>4	0.0 / 100.0	– / –
Quinupristin / dalfopristin	≤0.5 – 4	≤0.5	1	88.9 / 7.4	88.9 / 0.0
S.pneumoniae (2,150)					
Telavancin	≤0.015 – 0.12	≤0.015	0.03	– / –	– / –
Penicillin	≤0.03 – >4	≤0.03	4	87.6 / 0.6[e] / 61.9 / 2.4[f]	61.9 / 12.4
Vancomycin	≤0.12 – 1	0.25	0.5	100.0 / –	100.0 / 0.0
Linezolid	≤0.12 – 4	1	1	>99.9 / –	100.0 / 0.0
Levofloxacin	≤0.5 – >4	1	1	98.8 / 1.1	98.8 / 1.2
Erythromycin	≤0.25 – >4	≤0.25	>4	59.2 / 40.0	59.2 / 40.0
Clindamycin	≤0.25 – >1	≤0.25	>1	72.3 / 27.3	72.7 / 27.3
Tetracycline	≤0.25 – >8	0.5	>8	67.7 / 32.0	67.3 / 32.3
Viridans group streptococci (519)					
Telavancin	≤0.015 – 0.12	0.03	0.06	100.0 / –	
Penicillin	≤0.03 – >4	0.06	1	74.0 / 5.4	84.0 / 5.4
Vancomycin	≤0.12 – 1	0.5	0.5	100.0 / –	100.0 / 0.0
Teicoplanin	≤1	≤1	≤1	– / –	100.0 / 0.0
Daptomycin	≤0.06 – 2	0.25	0.5	99.6 / –	– / –
Linezolid	≤0.12 – 2	1	1	100.0 / –	– / –
Levofloxacin	≤0.5 – >4	1	2	92.5 / 6.2	– / –
Erythromycin	≤0.25 – >4	≤0.25	>4	52.2 / 45.1	– / –
Clindamycin	≤0.25 – >2	≤0.25	>2	86.9 / 12.1	87.9 / 12.1
β-hemolytic streptococci (1,472)					
Telavancin	≤0.015 – 0.25	0.06	0.12	99.8 / –	
Penicillin	≤0.03 – 0.12	≤0.03	0.06	100.0 / –	100.0 / 0.0
Vancomycin	≤0.12 – 1	0.5	0.5	100.0 / –	100.0 / 0.0
Teicoplanin	≤1	≤1	≤1	– / –	100.0 / 0.0
Daptomycin	≤0.06 – 0.5	≤0.06	0.25	100.0 / –	100.0 / 0.0
Linezolid	≤0.12 – 2	1	1	100.0 / –	100.0 / 0.0
Levofloxacin	≤0.5 – >4	≤0.5	1	98.4 / 1.3	94.7 / 1.6
Erythromycin	≤0.25 – >4	≤0.25	>4	75.3 / 23.6	75.3 / 23.6
Clindamycin	≤0.25 – >2	≤0.25	>2	87.5 / 12.0	88.0 / 12.0
S. bovis group (32)					
Telavancin	≤0.015 – 0.12	0.03	0.06	100.0 / –	
Penicillin	≤0.03 – 0.12	≤0.03	0.06	100.0 / 0.0	100.0 / 0.0
Vancomycin	0.25 – 0.5	0.25	0.5	100.0 / –	100.0 / 0.0
Teicoplanin	≤1	≤1	≤1	– / –	100.0 / 0.0
Daptomycin	≤0.06 – 0.12	≤0.06	≤0.06	100.0 / –	– / –
Linezolid	0.5 – 2	1	1	100.0 / –	– / –
Levofloxacin	≤0.5 – 2	1	2	100.0 / 0.0	– / –
Erythromycin	≤0.25 – >4	≤0.25	>4	59.4 / 37.5	– / –
Clindamycin	≤0.25 – >2	≤0.25	>2	75.0 / 25.0	75.0 / 25.0

MIC, minimum inhibitory concentration; MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative staphylococci.
[a]Criteria for susceptibility as published by the Clinical and Laboratory Standards Institute (M100-S21, 2011) and European Committee on Antimicrobial Susceptibility Testing (2011).
[b]For telavancin, the US FDA approved susceptible breakpoints for *S. aureus* (≤1 μg/mL), vancomycin-susceptible *E. faecalis* (≤1 μg/mL), viridans group streptococci (≤0.12 μg/mL), and β-hemolytic streptococci (≤0.12 μg/mL) were applied.
[c]–, no breakpoint available.
[d]Includes 32 and 6 VanA- and VanB-type strains, respectively.
[e]Penicillin parenteral (non-meningitis).
[f]Penicillin (oral penicillin V).

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