In Vitro Activity of Telavancin Against Gram-Positive Pathogens, Including Resistant Subsets: Results From a Global Surveillance Program (2007)

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ABSTRACT (REVISED)

Background. Telavancin (TLV) is a novel lipoglycopeptide targeting Gram-positive pathogens. An NDA has been submitted for complicated skin and skin structure infections and patient enrollment in Phase 3 studies for hospital-acquired pneumonia is complete. We evaluated the potency of TLV against a collection of recent Gram-positive isolates, including those with resistant (R) antibiograms.
Methods. 8649 non-duplicate clinical isolates of *Staphylococcus aureus*, *Enterococcus* spp., *Streptococcus pneumoniae*, viridans group streptococci (VGS), *Corynebacterium* spp. (n=15), *Turicella otitidis* (n=2), *Gemella* spp. (n=1), *Lactobacillus* spp. (n=2), *Micrococcus* spp. (n=3), and others (n=1714) were submitted from medical centers in North America (58.1%), Europe (32.4%), and Latin America (9.5%) participating in TLV surveillance for 2007 (**Table**). Identifications were confirmed by the central monitor and all isolates were susceptibility tested using Clinical and Laboratory Standard Institute methods.

	MIC (µg/mL)		Cumulative % inhibited at MIC				
Organism (n tested)	**50%**	**90%**	**≤0.12**	**0.25**	**0.5**	**1**	**2**
S. aureus (4522)	0.12	0.25	90	>99	100	–	–
OX-S (2384)	0.12	0.12	93	>99	100	–	–
OX-R (2138)	0.12	0.25	86	>99	100	–	–
Enterococcus spp. (1397)	0.25	2	33	70	81	84	95
VAN-S (VSE; 1088)	0.25	0.5	40	88	>99	100	–
VAN-R (VRE; 299)	2	>2	6	7	10	25	76
S. pneumoniae (863)	0.03	0.03	100	–	–	–	–
PEN-S (579)	0.03	0.03	100	–	–	–	–
PEN-NS (172)	0.03	0.03	100	–	–	–	–
PEN- & ERY-R (112)	0.03	0.03	100	–	–	–	–
VGS (130)	0.03	0.06	100	–	–	–	–
PEN-S (94)	0.03	0.06	100	–	–	–	–
PEN-NS (36)	0.03	0.06	100	–	–	–	–

ERY, erythromycin; NS, nonsusceptible; OX, oxacillin; PEN, penicillin; R, resistant; S, susceptible; VAN, vancomycin; VGS, viridans group streptococci; VRE, vancomycin-resistant enterococci; VSE, vancomycin-susceptible enterococci

Results. In the tested population, 47.3% of *S. aureus* were oxacillin-resistant, 21.4% of enterococci were vancomycin-resistant (VRE), 32.9% of *S. pneumoniae* were penicillin-nonsusceptible, and 27.7% of VGS were penicillin-nonsusceptible. TLV inhibited all *S. aureus* and vancomycin-susceptible enterococci at ≤1 µg/mL and all *S. pneumoniae* and VGS at ≤0.12 µg/mL. Only VRE displayed elevated TLV MIC values (MIC_{50}, 2 µg/mL; 24.4%, >2 µg/mL). Oxacillin-resistance among *S. aureus* and penicillin-nonsusceptibility among *S. pneumoniae* had no effect on TLV potency. Testing of penicillin-nonsusceptible VGS showed no difference versus penicillin-susceptible VGS. TLV MIC results for other tested Gram-positive pathogens were ≤0.03 µg/mL, with the exception of *Lactobacillus* spp. and *Micrococcus* spp. (≥2 µg/mL; also with vancomycin MICs ≥8 µg/mL).
Conclusions. TLV remained highly potent against year 2007 Gram-positive isolates, including resistant subsets. With the clinical introduction of TLV, continued monitoring for potential resistance emergence to it and currently marketed agents will be necessary.

Abstract updated to include additional isolates

INTRODUCTION

- Emergence of bacterial resistance is a significant global problem that complicates nosocomial infections, with increasing morbidity, mortality, and costs of hospitalization due to increased length of stay.
- Occurrence of methicillin-resistant *Staphylococcus aureus* (MRSA) is especially problematic in intensive care units. Furthermore, the dramatic spread of community-associated MRSA infections (e.g., USA-300 clone), including into the hospital environment, has created a public health emergency challenging traditional infection control practices.
- Increased usage of vancomycin in treating staphylococcal infections has resulted in a dramatic increase in vancomycin resistance among enterococci, especially *E. faecium*. Penicillin nonsusceptibility among strains of *Streptococcus pneumoniae* is also increasing, and currently exceeds 36% in the USA (higher elsewhere).
- The timely development and introduction of new agents active against these commonly occurring Gram-positive species are sorely needed.
- Telavancin is a novel, intravenous semi-synthetic lipoglycopeptide that is broadly active against both aerobic and anaerobic Gram-positive bacteria, including MRSA and some vancomycin-resistant enterococci (VRE).[1–5]
- The agent is rapidly bactericidal by means of interference with bacterial cell wall synthesis, similar to the glycopeptides, and also disruption of bacterial cell membrane function.[6]

- Recent success in Phase 2 and 3 complicated skin and skin structure clinical trials[7–9] have been followed by registration applications both in the USA and the European Union. Patient enrollment in Phase 3 trials for hospital-acquired pneumonia are complete.
- In this report, we summarize 2007 results to date of an international surveillance testing program comparing the activity of telavancin and currently marketed glycopeptides with other antimicrobial agents against staphylococcal, enterococcal, and streptococcal clinical isolates submitted from medical centers located in the USA, Latin America, and Europe. The analysis includes evaluation of resistant subsets for each of these groups. A total of 8649 bacterial strains were tested by reference Clinical and Laboratory Standards Institute (CLSI) methods with susceptibilities to comparator agents interpreted by CLSI breakpoint criteria.[10]

MATERIALS AND METHODS

Bacterial strain collection

- A total of 8649 non-duplicate consecutive Gram-positive clinical isolates were submitted from >60 medical centers located in North America, Latin America, and Europe as part of the international telavancin surveillance program for the first half of 2007.
- Isolates originated from patients with documented bloodstream (49.7%), respiratory tract (32.0%), or skin and soft tissue infections (18.3%). The distribution of leading species with emerging resistant subsets includes *S. aureus* (n=4522), coagulase-negative staphylococci (CoNS; n=873), *E. faecalis* (n=893), *E. faecium* (n=471), other *Enterococcus* spp. (n=20), *S. pneumoniae* (n=863), and viridans group streptococci (VGS; n=130) (**Table 1**).
- Identifications were confirmed by the central monitor (JMI Laboratories, Iowa, USA).

Susceptibility test methods

- All strains were tested by the broth microdilution method[11] using commercially validated and prepared panels (TREK Diagnostics, Cleveland, Ohio, USA) in cation-adjusted Mueller-Hinton broth (with 2–5% lysed horse blood added for testing of streptococci) against a variety of antimicrobial agents. These agents represented the most common classes and examples of drugs used in the empiric or directed treatment of the indicated pathogen.
- Interpretation of MIC results was in accordance with published CLSI criteria. Quality control strains utilized included *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619.

RESULTS

- In the tested population, 47.3% and 77.8% of *S. aureus* and CoNS, respectively, were oxacillin-resistant; 21.4% of enterococci were vancomycin-resistant, and 32.9% and 27.7% of *S. pneumoniae* and VGS, respectively, were penicillin nonsusceptible (**Table 2**).

- Telavancin inhibited all *S. pneumoniae*, VGS, and β-hemolytic streptococci at ≤0.25 µg/mL; all *S. aureus* and CoNS at ≤0.5 µg/mL, and all vancomycin-susceptible enterococci at ≤1 µg/mL.
- Among VRE, only 9.0% were susceptible to teicoplanin (MIC ≤8 µg/mL), whereas 75.6% had telavancin MIC values ≤2 µg/mL.
- Oxacillin-resistance among *S. aureus* and penicillin nonsusceptibility among *S. pneumoniae* and VGS had no effect on telavancin MIC_{50} potency compared with the respective susceptible strains.
- Telavancin MIC results for other tested Gram-positive pathogens (*Corynebacterium* spp., *Bacillus* spp., *Aerococcus* spp., *Turicella otitidis*, *Lactococcus* spp., and *Gemella* spp.) were ≤0.25 µg/mL, with the exception of the rarely-tested *Lactobacillus* spp., *Leuconostoc* spp. and *Micrococcus* spp. (>2 µg/mL; also with vancomycin MICs ≥8 µg/mL) (data not shown).

CONCLUSIONS

- Telavancin, a novel intravenous semi-synthetic lipoglycopeptide currently under registration review in the USA and European Union, remained highly potent against year 2007 Gram-positive isolates, inhibiting all *S. aureus* and CoNS at ≤0.5 µg/mL, all vancomycin-susceptible enterococci at ≤1 µg/mL, and all *S. pneumoniae*, VGS, and β-hemolytic streptococci at ≤0.25 µg/mL.
- While telavancin MIC values were elevated among VRE, 75.6% of strains had MIC values ≤2 µg/mL.
- Oxacillin-resistance among *S. aureus*, and penicillin nonsusceptibility among *S. pneumoniae* and VGS, had no effect on telavancin potency compared with respective susceptible strains.
- Pending regulatory approval and clinical introduction, continued monitoring for potential resistance emergence to telavancin and other Gram-positive-targeted agents will be necessary.

REFERENCES

1. Hegde SS et al. *Antimicrob Agents Chemother* 2004;48:3043–3050.
2. Goldstein EJ et al. *Antimicrob Agents Chemother* 2004;48:2149–2152.
3. Jansen WT et al. *Antimicrob Agents Chemother* 2007;51:3420–3424.
4. King A et al. *J Antimicrob Chemother* 2004;53:797–803.
5. Saravolatz LD et al. *J Antimicrob Chemother* 2007;60:406–409.
6. Higgins DL et al. *Antimicrob Agents Chemother* 2005;49:1127–1134.
7. Stryjewski ME et al. *Antimicrob Agents Chemother* 2006;50:862–867.
8. Stryjewski ME et al. *Clin Infect Dis* 2005;40:1601–1607.
9. Corey GR et al. *Clin Microbiol Infect* 2007;13(Suppl 1): Abstract P844.
10. Clinical and Laboratory Standards Institute. CLSI document M100-S17. Wayne, PA, USA, 2006.
11. Clinical and Laboratory Standards Institute. CLSI document M7-A7. Wayne, PA, USA, 2006.

Table 1. Antimicrobial activity of telavancin against six organism species/groups and resistant subsets submitted as part of the 2007 international surveillance program

	MIC (µg/mL)		Cumulative % inhibited at each telavancin MIC (µg/mL)							
Organism (n tested)	**50%**	**90%**	**≤0.015**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**
S. aureus (4522)	0.12	0.25	0	<1	10	90	>99	100	–	–
Oxacillin-susceptible (2384)	0.12	0.12	0	<1	12	93	>99	100	–	–
Oxacillin-resistant (2138)	0.12	0.25	0	<1	8	86	>99	100	–	–
Coagulase-negative staphylococci (873)	0.12	0.25	<1	1	17	89	>99	100	–	–
Oxacillin-susceptible (194)	0.12	0.12	<1	4	28	93	99	100	–	–
Oxacillin-resistant (679)	0.12	0.25	<1	<1	14	88	>99	100	–	–
Enterococcus spp. (1397)	0.25	2	<1	4	14	33	70	81	84	95
Vancomycin-susceptible (1088)	0.25	0.5	<1	5	16	40	88	>99	100	–
Vancomycin-resistant (299)	2	>2	0	<1	5	6	7	10	25	76
S. pneumoniae (863)	0.03	0.03	25	92	100	–	–	–	–	–
Penicillin-susceptible (579)	0.03	0.03	23	91	100	–	–	–	–	–
Penicillin-nonsusceptible (172)	0.03	0.03	30	92	100	–	–	–	–	–
Penicillin/erythromycin-resistant (112)	0.03	0.03	27	96	100	–	–	–	–	–
Viridans group streptococci (130)	0.03	0.06	6	70	>99	100	–	–	–	–
Penicillin-susceptible (94)	0.03	0.06	6	69	99	100	–	–	–	–
Penicillin-nonsusceptible (36)	0.03	0.06	6	72	100	–	–	–	–	–
β-hemolytic streptococci (468)	0.03	0.06	4	54	98	>99	100	–	–	–

Table 2. Antimicrobial activity of telavancin and comparator antimicrobial agents against year 2007 Gram-positive isolates

Organism (n tested)/ antimicrobial agent	MIC_{50}	MIC_{90}	Range	% susceptible/ resistant[a]
S. aureus (4522)				
Telavancin	0.12	0.25	0.03–0.5	–/–
Vancomycin	1	1	≤0.12–4	>99.9/0.0
Teicoplanin	≤2	≤2	≤2–16	>99.9/0.0
Daptomycin	0.25	0.5	≤0.06–2	>99.9/–
Linezolid	1	2	0.25–>8	>99.9/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–>2	99.8/0.1
Levofloxacin	≤0.5	>4	≤0.5–>4	60.0/39.6
Erythromycin	>4	>4	≤0.25–>4	45.3/54.4
Clindamycin	≤0.25	>2	≤0.25–>2	79.1/20.8
Tetracycline	≤2	≤2	≤2–>8	94.6/5.1
Oxacillin	1	>2	≤0.25–>2	52.7/47.3
Oxacillin-susceptible (2384)				
Telavancin	0.12	0.12	0.03–0.5	–/–
Vancomycin	1	1	≤0.12–2	100.0/0.0
Teicoplanin	≤2	≤2	≤2–4	100.0/0.0
Daptomycin	0.25	0.25	≤0.06–1	100.0/–
Linezolid	1	2	0.25–2	100.0/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–2	99.9/0.0
Levofloxacin	≤0.5	≤0.5	≤0.5–>4	92.5/7.3
Erythromycin	≤0.25	>4	≤0.25–>4	76.0/23.6
Clindamycin	≤0.25	≤0.25	≤0.25–>2	96.1/3.8
Tetracycline	≤2	≤2	≤2–>8	96.1/3.5
Oxacillin	0.5	0.5	≤0.25–2	100.0/0.0
Oxacillin-resistant (2138)				
Telavancin	0.12	0.25	0.03–0.5	–/–
Vancomycin	1	1	0.25–4	>99.9/0.0
Teicoplanin	≤2	≤2	≤2–16	>99.9/0.0
Daptomycin	0.25	0.5	≤0.06–2	99.9/–
Linezolid	1	2	0.25–>8	99.9/–
Quinupristin/dalfopristin	0.5	0.5	≤0.25–>2	99.6/0.2
Levofloxacin	>4	>4	≤0.5–>4	23.8/75.6
Erythromycin	>4	>4	≤0.25–>4	11.0/88.7
Clindamycin	≤0.25	>2	≤0.25–>2	60.1/39.8
Tetracycline	≤2	≤2	≤2–>8	93.0/6.8
Oxacillin	>2	>2	>2	0.0/100.0
Coagulase-negative staphylococci (873)				
Telavancin	0.12	0.25	≤0.015–0.5	–/–
Vancomycin	1	2	≤0.12–8	99.9/0.0
Teicoplanin	≤2	4	≤2–>16	99.4/0.1
Daptomycin	0.25	0.5	≤0.06–4	99.8/–
Linezolid	0.5	1	≤0.06–>8	99.1/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–>2	99.4/0.3
Levofloxacin	4	>4	≤0.5–>4	41.0/55.3
Erythromycin	>4	>4	≤0.25–>4	31.3/68.6
Clindamycin	≤0.25	>2	≤0.25–>2	65.2/33.4
Tetracycline	≤2	>8	≤2–>8	85.0/13.9
Oxacillin	>2	>2	≤0.25–>2	22.2/77.8
Oxacillin-susceptible (194)				
Telavancin	0.12	0.12	≤0.015–0.5	–/–
Vancomycin	1	2	0.25–2	100.0/0.0
Teicoplanin	≤2	≤2	≤2–8	100.0/0.0
Daptomycin	0.25	0.5	≤0.06–1	100.0/–
Linezolid	1	1	≤0.06–>8	99.5/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–0.5	100.0/0.0
Levofloxacin	≤0.5	4	≤0.5–>4	87.6/12.4
Erythromycin	≤0.25	>4	≤0.25–>4	58.2/41.8
Clindamycin	≤0.25	≤0.25	≤0.25–>2	92.8/5.7
Tetracycline	≤2	>8	≤2–>8	88.1/10.3
Oxacillin	≤0.25	≤0.25	≤0.25	100.0/0.0
Oxacillin-resistant (679)				
Telavancin	0.12	0.25	≤0.015–0.5	–/–
Vancomycin	1	2	≤0.12–8	99.9/0.0
Teicoplanin	≤2	4	≤2–>16	99.3/0.1
Daptomycin	0.25	0.5	≤0.06–4	99.7/–
Linezolid	0.5	1	≤0.06–>8	99.0/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–>2	99.3/0.4
Levofloxacin	>4	>4	≤0.5–>4	27.7/67.6
Erythromycin	>4	>4	≤0.25–>4	23.6/76.3
Clindamycin	≤0.25	>2	≤0.25–>2	57.3/41.4
Tetracycline	≤2	>8	≤2–>8	84.1/14.9
Oxacillin	>2	>2	0.5–>2	0.0/100.0
Enterococcus spp. (1397)				
Telavancin	0.25	2	≤0.015–>2	–/–
Vancomycin	1	>16	≤0.12–>16	77.9/21.4
Teicoplanin	≤2	>16	≤2–>16	80.4/17.6
Daptomycin	1	2	≤0.06–4	100.0/–
Linezolid	1	2	0.25–>8	99.4/0.6
Quinupristin/dalfopristin	>2	>2	≤0.25–>2	28.2/66.1
Levofloxacin	>4	>4	≤0.5–>4	45.3/54.0
Gentamicin (HL)	≤500	>1000	≤500–>1000	69.3/30.7
Streptomycin (HL)	≤1000	>2000	≤1000–>2000	68.4/31.6
Tetracycline	>8	>8	≤2–>8	43.0/57.0
Ampicillin	≤1	>16	≤1–>16	68.6/31.4
Vancomycin-susceptible (1088)				
Telavancin	0.25	0.5	≤0.015–1	–/–
Vancomycin	1	2	≤0.12–4	100.0/0.0
Teicoplanin	≤2	≤2	≤2–>16	99.8/0.2
Daptomycin	1	2	≤0.06–4	100.0/–
Linezolid	1	2	0.25–>8	99.8/0.2
Quinupristin/dalfopristin	>2	>2	≤0.25–>2	12.9/81.3
Levofloxacin	2	>4	≤0.5–>4	57.8/41.3
Gentamicin (HL)	≤500	>1000	≤500–>1000	70.7/29.3
Streptomycin (HL)	≤1000	>2000	≤1000–>2000	69.8/30.2
Tetracycline	>8	>8	≤2–>8	36.9/63.1
Ampicillin	≤1	>16	≤1–>16	85.2/14.8

Table 2 (continued). Antimicrobial activity of telavancin and comparator antimicrobial agent against year 2007 Gram-positive isolates

Organism (n tested)/ antimicrobial agent	MIC_{50}	MIC_{90}	Range	% susceptible/ resistant[a]
Vancomycin-resistant (299)				
Telavancin	2	>2	0.03–>2	–/–
Vancomycin	>16	>16	>16	0.0/100.0
Teicoplanin	>16	>16	≤2–>16	9.0/81.6
Daptomycin	1	2	0.25–4	100.0/–
Linezolid	1	2	0.5–>8	98.0/2.0
Quinupristin/dalfopristin	0.5	>2	≤0.25–>2	82.9/12.0
Levofloxacin	>4	>4	2–>4	0.3/99.7
Gentamicin (HL)	≤500	>1000	≤500–>1000	63.9/36.1
Streptomycin (HL)	≤1000	>2000	≤1000–>2000	62.9/37.1
Tetracycline	≤2	>8	≤2–>8	63.9/36.1
Ampicillin	>16	>16	≤1–>16	9.4/90.6
S. pneumoniae (863)				
Telavancin	0.03	0.03	≤0.015–0.06	–/–
Vancomycin	≤1	≤1	≤1	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.12	0.12	≤0.06–0.5	–/–
Linezolid	1	1	≤0.12–2	100.0/–
Quinupristin/dalfopristin	0.5	0.5	≤0.25–1	100.0/0.0
Levofloxacin	1	1	≤0.5–>4	99.3/0.6
Erythromycin	≤0.25	>2	≤0.25–>2	66.2/33.5
Clindamycin	≤0.25	>2	≤0.25–>2	83.1/16.7
Tetracycline	≤2	>8	≤2–>8	78.1/21.4
Penicillin	≤0.03	2	≤0.03–8	67.1/17.3
Penicillin-susceptible (579)				
Telavancin	0.03	0.03	≤0.015–0.06	–/–
Vancomycin	≤1	≤1	≤1	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.12	0.12	≤0.06–0.5	–/–
Linezolid	1	1	≤0.12–2	100.0/–
Quinupristin/dalfopristin	0.5	0.5	≤0.25–1	100.0/0.0
Levofloxacin	1	1	≤0.5–>4	99.1/0.9
Erythromycin	≤0.25	>2	≤0.25–>2	83.9/15.5
Clindamycin	≤0.25	≤0.25	≤0.25–>2	95.9/4.1
Tetracycline	≤2	≤2	≤2–>8	91.2/8.3
Penicillin	≤0.03	≤0.03	≤0.03–0.06	100.0/0.0
Penicillin-nonsusceptible (172)				
Telavancin	0.03	0.03	≤0.015–0.06	–/–
Vancomycin	≤1	≤1	≤1	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.12	0.12	≤0.06–0.25	–/–
Linezolid	1	1	≤0.12–2	100.0/–
Quinupristin/dalfopristin	0.5	0.5	≤0.25–0.5	100.0/0.0
Levofloxacin	1	1	≤0.5–2	100.0/0.0
Erythromycin	1	>2	≤0.25–>2	49.4/50.6
Clindamycin	≤0.25	>2	≤0.25–>2	72.7/26.7
Tetracycline	≤2	>8	≤2–>8	69.8/30.2
Penicillin	0.25	2	0.12–4	0.0/21.5
Viridans group streptococci (130)				
Telavancin	0.03	0.06	≤0.015–0.12	–/–
Vancomycin	0.5	1	≤0.12–1	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.25	0.5	≤0.06–1	100.0/–
Linezolid	0.5	1	0.12–2	100.0/–
Quinupristin/dalfopristin	0.5	1	≤0.25–2	99.2/0.0
Levofloxacin	1	2	≤0.5–>4	96.9/2.3
Erythromycin	0.5	>2	≤0.25–>2	47.7/50.0
Clindamycin	≤0.25	0.5	≤0.25–>2	89.1/9.2
Tetracycline	≤2	>8	≤2–>8	68.5/28.5
Penicillin	0.06	2	≤0.015–32	72.3/6.9
Penicillin-susceptible (94)				
Telavancin	0.03	0.06	≤0.015–0.12	–/–
Vancomycin	0.5	1	≤0.12–1	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.25	0.5	≤0.06–1	100.0/–
Linezolid	0.5	1	0.12–2	100.0/–
Quinupristin/dalfopristin	0.5	1	≤0.25–1	100.0/0.0
Levofloxacin	1	2	≤0.5–>4	95.7/3.2
Erythromycin	≤0.25	>2	≤0.25–>2	56.4/41.5
Clindamycin	≤0.25	≤0.25	≤0.25–>2	90.4/7.4
Tetracycline	≤2	>8	≤2–>8	72.3/25.5
Penicillin	0.03	0.12	≤0.015–0.12	100.0/0.0
Penicillin-nonsusceptible (36)				
Telavancin	0.03	0.06	≤0.015–0.06	–/–
Vancomycin	0.5	0.5	0.25–0.5	100.0/–
Teicoplanin	≤2	≤2	≤2	–/–
Daptomycin	0.25	0.5	≤0.06–1	100.0/–
Linezolid	0.5	1	≤0.25–2	97.2/0.0
Quinupristin/dalfopristin	0.5	1	≤0.25–2	97.2/0.0
Levofloxacin	1	1	≤0.5–2	100.0/0.0
Erythromycin	2	>2	≤0.25–>2	25.0/72.2
Clindamycin	≤0.25	>2	≤0.25–>2	86.1/13.9
Tetracycline	≤2	>8	≤2–>8	58.3/36.1
Penicillin	0.5	8	0.25–32	0.0/25.0
β-hemolytic streptococci (468)				
Telavancin	0.03	0.06	≤0.015–0.25	–/–
Vancomycin	0.5	0.5	0.25–1	100.0/–
Teicoplanin	≤2	≤2	≤2–4	–/–
Daptomycin	≤0.06	0.25	≤0.06–0.25	100.0/–
Linezolid	1	1	0.25–2	100.0/–
Quinupristin/dalfopristin	≤0.25	0.5	≤0.25–1	100.0/0.0
Levofloxacin	≤0.5	1	≤0.5–>4	99.4/0.4
Erythromycin	≤0.25	>2	≤0.25–>2	81.2/18.2
Clindamycin	≤0.25	≤0.25	≤0.25–>2	91.2/8.5
Tetracycline	≤2	>8	≤2–>8	51.5/46.8
Penicillin	≤0.015	0.06	≤0.015–0.12	100.0/–

a. Criteria as published by the CLSI [2007]