Delafloxacin activity tested against bacterial pathogens from 44 medical centres in Europe and Israel (2014)

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ABSTRACT

Background: Delafloxacin is an investigational anionic fluoroquinolone antibiotic currently in phase III development in the United States for the treatment of acute bacterial skin and skin structure infections. It is active against Gram-positive and -negative bacteria including anaerobes and atypical bacteria. Included in its activity spectrum are fluoroquinolone- and methicillin-resistant staphylococci. The aim of this study was to examine the susceptibility profiles of delafloxacin when tested against contemporary clinical isolates collected from medical centres in Europe and Israel during 2014.

Methods: A total of 2,075 Gram-positive and -negative, non-duplicate, non-consecutive, bacterial clinical isolates collected from patients in 44 medical centres across >20 European countries and Israel were selected. Isolate identity was confirmed at a central monitoring laboratory using standard bacteriologic algorithms and the use of MALDI-TOF-MS when necessary. Antibacterial susceptibility testing was performed by broth microdilution per CLSI guidelines. EUCAST breakpoints were used to determine susceptibility rates.

Results: The delafloxacin $MIC_{50/90}$ for all *S. aureus* was ≤0.004/0.12 mg/L. Delafloxacin was the most potent ($MIC_{50/90}$, ≤0.004/≤0.004 mg/L) antimicrobial tested against MSSA and based on MIC_{90} was at least 64-fold more potent than ceftaroline and levofloxacin. Delafloxacin ($MIC_{50/90}$, 0.12/0.25 mg/L), tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L), daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), and trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 mg/L) were the most potent antimicrobials tested against MRSA; susceptibility to vancomycin ($MIC_{50/90}$, 1/1 mg/L) and linezolid ($MIC_{50/90}$, 0.5/1 mg/L) was 100.0%. There were high levels of resistance against levofloxacin (73.4% resistant) and erythromycin (64.1%). Delafloxacin ($MIC_{50/90}$, 0.06/1 mg/L) and linezolid ($MIC_{50/90}$, 1/1 mg/L) were the most active antimicrobials tested against *Enterococcus faecalis*. Against *Streptococcus pneumoniae*, delafloxacin was the most active agent ($MIC_{50/90}$, 0.008/0.015 mg/L; highest MIC, 0.03 mg/L). Delafloxacin was eight-fold more active than ceftaroline ($MIC_{50/90}$, ≤0.015/0.12 mg/L; 98.7% susceptible); 16-fold more active than moxifloxacin ($MIC_{50/90}$, ≤0.12/0.25 mg/L; 100.0% susceptible), and 64-fold more active than levofloxacin ($MIC_{50/90}$, 1/1 mg/L; 100.0% susceptible). Delafloxacin was active against β-hemolytic streptococci (MIC_{90}, 0.015 mg/L). Overall, against 750 Enterobacteriaceae, the delafloxacin $MIC_{50/90}$ was 0.06/4 mg/L with 78.3% of isolates inhibited at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were 77.1 and 80.9%, respectively and ceftazidime susceptibility was 77.2%. Delafloxacin inhibited 73.0% of *Pseudomonas aeruginosa* at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibility rates were 66.0 and 62.0%, respectively. Colistin was the only agent which exhibited at least 90% susceptibility. Delafloxacin inhibited 29.0% of *Acinetobacter baumannii* at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were poor (17.0%). Colistin (90.0% susceptible) was the only agent to achieve susceptibility ≥90%.

Conclusions: Delafloxacin provides a number of *in vitro* advantages in potency and spectrum when directly compared to currently marketed fluoroquinolones, especially with its enhanced activity against *S. aureus*, including MRSA strains, and its improved potency against *S. pneumoniae,* β-hemolytic streptococci, and *E. faecalis.* Further evaluation in clinical trials appears warranted.

INTRODUCTION

Delafloxacin is an investigational anionic fluoroquinolone antibiotic currently in phase III development for the treatment of acute bacterial skin and skin structure infections (ABSSSI). Unlike other quinolones which usually have a binding preference for DNA gyrase or topoisomerase IV, delafloxacin is equally potent against both. This dual targeting is believed to help reduce the selection of resistant mutants *in vitro* and *in vivo*. Additionally, the anionic structure of delafloxacin may enhance its potency in acidic environments which is characteristic of the milieu at an infection site.

Delafloxacin is active against a broad range of Gram-positive and Gram-negative bacteria including anaerobes and atypical bacteria (*Chlamydia* and *Mycoplasma*). It has been shown to be highly active against pathogens which are found in ABSSSI including fluoroquinolone-resistant staphylococci (methicillin-resistant *S. aureus* [MRSA] and methicillin-resistant coagulase-negative staphylococci [MR-CoNS]), β-hemolytic streptococci, Enterobacteriaceae, *Pseudomonas aeruginosa*, and anaerobes. Delafloxacin is also active against bacteria associated with respiratory tract infections (hospital and community-acquired respiratory infections) including activity against fluoroquinolone-resistant *Streptococcus pneumoniae*.

The aim of this study was to examine the susceptibility profiles and antibiograms of delafloxacin when tested against 2,075 contemporary clinical isolates collected from European medical centres during surveillance year 2014.

MATERIALS AND METHODS

Strain collection: Bacterial isolates were identified by the submitting laboratories and confirmed by JMI Laboratories using standard bacteriologic algorithms and methodologies, including the use of MALDI-TOF-MS (Bruker Daltonics, Bremen, Germany), when necessary. Bacterial isolates (non-duplicate; 2,075 isolates) were collected prospectively from medical centres for the year 2014. Countries (numbers of medical centres): Austria (1), Belgium (1), Czech Republic (1), Denmark (1), Finland (1), France (4), Germany (5), Greece (1), Hungary (1), Ireland (2), Israel (1), Italy (4), Netherlands (1), Norway (1), Poland (1), Portugal (1), Romania (1), Russia (3), Slovenia (1), Spain (3), Sweden (2), Switzerland (1), Turkey (2), United Kingdom (3), Ukraine (1). Isolates were collected from patients with bloodstream (BSI), community-acquired and hospital respiratory tract, ABSSSI, and other infections. The largest numbers of isolates were from BSI (625), ABSSSI (496), and respiratory (hospital; 338) infections. These three specimen sources represented 70.3% of all isolates.

Susceptibility testing: Susceptibility testing was performed using validated broth microdilution (CLSI M07-A10 (2015)). Panels were produced by Thermo Fisher Scientific (Cleveland, Ohio, USA). Interpretive criteria used were those of EUCAST (2015). CLSI interpretive criteria are provided in the MIC summary tables for informational purposes (M100-S25; 2015). All *Escherichia coli* and *Klebsiella* spp. isolates for which ceftriaxone or ceftazidime or aztreonam were ≥2 mg/L were considered to be screen-positive for ESBL production (CLSI, 2015). Quality control (QC) strains were tested concurrently and included *E. coli* ATCC 25922 and 35218, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619.

RESULTS

- Delafloxacin was very active against all tested *S. aureus* (MIC_{90}, 0.12 mg/L) and CoNS (MIC_{90}, 0.25 mg/L; **Table 1**).
- The most potent antimicrobial tested against MSSA was delafloxacin ($MIC_{50/90}$, ≤0.004/≤0.004 mg/L). Based on MIC_{90}, delafloxacin was at least 64-fold more potent than ceftaroline and levofloxacin (**Table 2**).
- Against MRSA isolates tested, tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L), delafloxacin ($MIC_{50/90}$, 0.12/0.25 mg/L) and daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L) were the most potent antimicrobials (**Table 2**). Delafloxacin was at least 64-fold more potent than levofloxacin (by MIC_{50}) and at least 32-fold more potent by MIC_{90} (**Table 2**).
- MRSA exhibited high levels of resistance against levofloxacin (73.4% resistant) and erythromycin (64.1%; **Table 2**). The greatest coverage of all *S. aureus* (MSSA and MRSA) was provided by daptomycin, linezolid, tigecycline, and vancomycin (100.0% susceptible; **Table 2**). Trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 mg/L) provided 99.2% coverage and ceftaroline ($MIC_{50/90}$, 0.25/1 mg/L) 96.4% coverage (data not shown). All *S. aureus* isolates were inhibited by delafloxacin at ≤2 mg/L (99.6% at ≤1 mg/L; **Table 1**).
- The majority of *E. faecalis* isolates exhibited relatively low delafloxacin MIC results ($MIC_{50/90}$, 0.06/1 mg/L) contrasting with *E. faecium* MIC values ($MIC_{50/90}$, >4/>4 mg/L) (**Table 1**). There were two vancomycin-resistant *E. faecalis,* both of which exhibited a delafloxacin MIC of 0.5 mg/L. There were 24 vancomycin-resistant *E. faecium* (24%), delafloxacin MIC values ranged from 4->4 mg/L.
- Delafloxacin was the most active agent tested against *S. pneumoniae* ($MIC_{50/90}$, 0.008/0.015 mg/L; **Table 1**). All isolates were inhibited at a delafloxacin MIC of ≤0.03 mg/L (**Table 1**). Delafloxacin was eight-fold more active than ceftaroline ($MIC_{50/90}$, ≤0.015/0.12 mg/L; 98.7% susceptible), 16-fold more active than moxifloxacin ($MIC_{50/90}$, ≤0.12/0.25 mg/L; 100.0% susceptible), and 64-fold more active than levofloxacin (1/1 mg/L; 100.0% susceptible; **Table 2**).
- Delafloxacin ($MIC_{50/90}$, 0.015/0.06 mg/L) was the most active agent tested viridans group streptococci (comparator data not shown).
- Highly potent activity against *S. pyogenes*, S. *agalactiae*, and *S. dysgalactiae* was exhibited by delafloxacin. All delafloxacin MIC values for *S. pyogenes* and for *S. dysgalactiae* were ≤0.03 mg/L. For *S. agalactiae*, 96.0% of isolates were inhibited at a delafloxacin MIC of ≤0.03 mg/L and the highest MIC was 0.25 mg/L (**Table 1**)
- Delafloxacin was active against the majority of Enterobacteriaceae, exhibiting $MIC_{50/90}$ values of 0.06/4 mg/L with 78.3% of isolates inhibited at a delafloxacin concentration of ≤1 mg/L (**Table 1**).
- Fluoroquinolone susceptibility as tested by ciprofloxacin and levofloxacin for Enterobacteriaceae ranged from 77.1-80.9% (**Table 3**)
- Against ESBL-producing enteric bacilli, fluoroquinolone activity was reduced. Against ESBL-phenotype *E. coli*, 30.0% of isolates were inhibited at ≤1 mg/L of delafloxacin and against ESBL-phenotype *K. pneumoniae*, 16.4% were inhibited at ≤1 mg/L (**Table 1**).
- Delafloxacin was active against species with high rates of ceftazidime resistance due to AmpC production, including *Enterobacter* spp., *Citrobacter* spp., and *Serratia* spp. isolates. Delafloxacin inhibited 87.4% of *Enterobacter* spp. isolates at ≤1 mg/L. Against *Citrobacter* spp., a total of 88.3% of isolate MIC values were at ≤1 mg/L and for *Serratia* spp., 73.8% were inhibited at ≤1 mg/L (data not shown).
- Delafloxacin inhibited 73.0% of *P. aeruginosa* at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were 66.0 and 62.0%, respectively (**Table 3**).
- The activity of delafloxacin against *Acinetobacter* spp. isolates was limited, with 29.0% of isolates inhibited at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were each 17.0% (**Table 3**).

CONCLUSIONS

- Delafloxacin was shown to exhibit broad-spectrum *in vitro* activity against contemporary Gram-positive and Gram-negative bacteria from Europe.
- Delafloxacin offers a number of advantages in *in vitro* potency and spectrum when compared to currently marketed fluoroquinolone agents especially with its enhanced activity against *S. aureus* and CoNS, including methicillin-resistant strains, and its improved potency against *S. pneumoniae* and β-hemolytic streptococci.
- The results of this investigation support the value of further study of the use of delafloxacin in infections where the above mentioned organisms may be found including community-acquired pneumonia and skin and soft tissue infections.

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Table 1. MIC (mg/L) distributions and cumulative frequency (%) for delafloxacin (Europe, 2014)

Organism	Count	≤0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4	MIC_{50}	MIC_{90}
Staphylococcus aureus	250	193 (77.2)	2 (78.0)	1 (78.4)	4 (80.0)	12 (84.8)	13 (90.0)	18 (97.2)	3 (98.4)	3 (99.6)	1 (100.0)	--	--	≤0.004	0.12
MSSA	186	176 (94.6)	2 (95.7)	1 (96.2)	2 (97.3)	1 (97.8)	2 (98.9)	1 (99.5)	0 (99.5)	1 (100.0)	--	--	--	≤0.004	≤0.004
MRSA	64	17 (26.6)	0 (26.6)	0 (26.6)	2 (29.7)	11 (46.9)	11 (64.1)	17 (90.6)	3 (95.3)	2 (98.4)	1 (100.0)	--	--	0.12	0.25
Coagulase-negative staphylococci	100	43 (43.0)	8 (51.0)	1 (52.0)	6 (58.0)	10 (68.0)	10 (78.0)	14 (92.0)	5 (97.0)	3 (100.0)	--	--	--	0.008	0.25
MRCoNS	67	18 (26.9)	2 (29.9)	0 (29.9)	6 (38.8)	9 (52.2)	10 (67.2)	14 (88.1)	5 (95.5)	3 (100.0)	--	--	--	0.06	0.5
Enterococcus faecalis	150	2 (1.3)	2 (2.7)	0 (2.7)	16 (13.3)	57 (51.3)	31 (72.0)	3 (74.0)	17 (85.3)	22 (100.0)	--	--	--	0.06	1
Enterococcus faecium	100	--	1 (1.0)	1 (2.0)	0 (2.0)	0 (2.0)	0 (2.0)	2 (4.0)	1 (5.0)	2 (7.0)	1 (8.0)	7 (15.0)	85 (100.0)	>4	>4
Streptococcus pneumoniae	150	16 (10.7)	90 (70.7)	40 (97.3)	4 (100.0)	--	--	--	--	--	--	--	--	0.008	0.015
penicillin-resistant (>4 mg/L)	1	--	1 (100.0)	--	--	--	--	--	--	--	--	--	--	--	--
Viridans group streptococci	100	20 (20.0)	19 (39.0)	30 (69.0)	19 (88.0)	8 (96.0)	0 (96.0)	3 (99.0)	1 (100.0)	--	--	--	--	0.015	0.06
Streptococcus pyogenes	150	33 (22.0)	94 (84.7)	20 (98.0)	3 (100.0)	--	--	--	--	--	--	--	--	0.008	0.015
Streptococcus agalactiae	75	5 (6.7)	38 (57.3)	28 (94.7)	1 (96.0)	1 (97.3)	1 (98.7)	1 (100.0)	--	--	--	--	--	0.008	0.015
Streptococcus dysgalactiae	50	18 (36.0)	30 (96.0)	1 (98.0)	1 (100.0)	--	--	--	--	--	--	--	--	0.008	0.008
Enterobacteriaceae	750	1 (0.1)	11 (1.6)	81 (12.4)	118 (28.1)	196 (54.3)	76 (64.4)	25 (67.7)	30 (71.7)	49 (78.3)	64 (86.8)	44 (92.7)	55 (100.0)	0.06	4
Escherichia coli	200	1 (0.5)	9 (5.0)	61 (35.5)	43 (57.0)	14 (64.0)	8 (68.0)	9 (72.5)	2 (73.5)	6 (76.5)	24 (88.5)	16 (96.5)	7 (100.0)	0.03	4
non-ESBL-phenotype	160	1 (0.6)	9 (6.2)	58 (42.5)	39 (66.9)	14 (75.6)	7 (80.0)	7 (84.4)	2 (85.6)	4 (88.1)	13 (96.2)	5 (99.4)	1 (100.0)	0.03	2
ESBL-phenotype	40	--	--	3 (7.5)	4 (17.5)	0 (17.5)	1 (20.0)	2 (25.0)	0 (25.0)	2 (30.0)	11 (57.5)	11 (85.0)	6 (100.0)	2	>4
Klebsiella pneumoniae	164	--	--	1 (0.6)	12 (7.9)	64 (47.0)	14 (55.5)	2 (56.7)	5 (59.8)	7 (64.0)	10 (70.1)	17 (80.5)	32 (100.0)	0.12	>4
non-ESBL-phenotype	97	--	--	1 (1.0)	12 (13.4)	60 (75.3)	12 (87.6)	2 (89.7)	4 (93.8)	3 (96.9)	2 (99.0)	0 (99.0)	1 (100.0)	0.06	0.5
ESBL-phenotype	67	--	--	--	--	4 (6.0)	2 (9.0)	0 (9.0)	1 (10.4)	4 (16.4)	8 (28.4)	17 (53.7)	31 (100.0)	4	>4
Enterobacter spp.	95	--	--	1 (1.1)	14 (15.8)	51 (69.5)	11 (81.1)	3 (84.2)	2 (86.3)	1 (87.4)	7 (94.7)	1 (95.8)	4 (100.0)	0.06	2
Pseudomonas aeruginosa	100	--	--	--	1 (1.0)	3 (4.0)	22 (26.0)	28 (54.0)	11 (65.0)	8 (73.0)	1 (74.0)	7 (81.0)	19 (100.0)	0.25	>4
Acinetobacter baumannii-calcoaceticus species complex	100	--	--	--	3 (3.0)	8 (11.0)	5 (16.0)	1 (17.0)	5 (22.0)	7 (29.0)	18 (47.0)	27 (74.0)	26 (100.0)	4	>4

Table 2. Activity of delafloxacin and comparator antimicrobial agents against Gram-positive bacteria (Europe, 2014)

Antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S / %R	EUCAST[a] %S / %R
MRSA (64)				
Delafloxacin	0.12	0.25	-	-
Levofloxacin	>4	>4	26.6/73.4	26.6/73.4
Ceftaroline	1	2	85.9/0.0	85.9/14.1
Clindamycin	≤0.25	>2	81.2/18.8	81.2/18.8
Daptomycin	0.25	0.5	100.0/-	100.0/0.0
Erythromycin	16	>16	35.9/56.2	35.9/64.1
Linezolid	0.5	1	100.0/0.0	100.0/0.0
Oxacillin	>2	>2	0.0/100.0	0.0/100.0
Tetracycline	≤0.5	>8	79.7/15.6	79.7/20.3
Tigecycline	0.06	0.12	100.0/-[b]	100.0/0.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	100.0/0.0	100.0/0.0
Vancomycin	1	1	100.0/0.0	100.0/0.0
MSSA (186)				
Delafloxacin	≤0.004	≤0.004	-	-
Levofloxacin	0.25	0.25	95.2/4.3	95.2/4.3
Ceftaroline	0.25	0.25	100.0/0.0	100.00.0
Clindamycin	≤0.25	≤0.25	97.3/2.2	96.2/2.7
Daptomycin	0.25	0.25	100.0/-	100.0/0.0
Erythromycin	0.25	>16	86.0/11.8	86.0/13.4
Linezolid	1	1	100.0/0.0	100.0/0.0
Oxacillin	0.5	0.5	100.0/0.0	100.0/0.0
Tetracycline	≤0.5	≤0.5	93.5/5.4	93.5/6.5
Tigecycline	0.06	0.06	100.0/ -[b]	100.0/0.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	98.9/1.1	98.9/0.5
Vancomycin	1	1	100.0/0.0	100.0/0.0

Antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S / %R	EUCAST[a] %S / %R
Enterococcus faecalis (150)				
Delafloxacin	0.06	1	-	-
Levofloxacin	1	>4	66.7/32.7	-
Ampicillin	1	2	100.0/0.0	99.3/0.0
Daptomycin	1	2	100.0/-	-
Erythromycin	>16	>16	6.0/52.7	-
Linezolid	1	1	100.0/0.0	100.0/0.0
Teicoplanin	≤2	≤2	98.0/2.0	98.0/2.0
Tetracycline	>8	>8	23.3/76.7	-
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	-	0.0/80.0
Vancomycin	1	2	98.7/1.3	98.7/1.3
S. pneumoniae (150)				
Delafloxacin	0.008	0.015	-	-
Levofloxacin	1	1	100.0/0.0	100.0/0.0
Moxifloxacin	≤0.12	0.25	100.0/0.0	100.0/0.0
Amoxicillin-clavulanate	≤1	2	92.0/4.7[c]	-
Ceftaroline	≤0.015	0.12	99.3/-	98.7/1.3
Ceftriaxone	≤0.06	1	84.0/6.0[d]	84.0/1.3
			94.0/1.3[c]	-
Clindamycin	≤0.25	>2	84.7/15.3	84.7/15.3
Erythromycin	≤0.12	>16	75.8/24.2	75.8/24.2
Meropenem	≤0.015	0.5	87.3/4.0	87.3/ 0.7[d]
			-	100.0/0.0[c]
Penicillin	≤0.06	1	72.0/ 10.0[e]	72.0/28.0[d]
			72.0/28.0[f]	72.0/5.3[c]
			94.7/ 0.7[g]	-
Tetracycline	≤0.5	>8	80.0/20.0	80.0/20.0
Trimethoprim-sulfamethoxazole	≤0.5	>4	68.0/20.0	74.0/20.0

a. Criteria as published by CLSI [2015] and EUCAST [2015]
b. Breakpoints from FDA Packet Insert revised 12/2014
c. Using Non Meningitis breakpoints
d. Using Meningitis breakpoints
e. Using Oral breakpoints
f. Using Parenteral, Meningitis breakpoints
g. Using Parenteral, Non Meningitis breakpoints

Table 3. Activity of delafloxacin and comparator antimicrobial agents against Gram-negative bacteria (Europe, 2014)

Antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S / %R	EUCAST[a] %S / %R
Enterobacteriaceae (750)[b]				
Delafloxacin	0.06	4	-	-
Ciprofloxacin	≤0.03	>4	79.3/18.1	77.1/20.7
Levofloxacin	≤0.12	>4	82.9/14.9	80.9/17.1
Ampicillin-sulbactam	16	>32	42.8/40.5	42.8/57.2
Aztreonam	≤0.12	>16	81.1/16.7	78.0/18.9
Cefepime	≤0.5	16	85.8/11.1[c]	82.8/12.3
Ceftazidime	0.25	32	81.5/16.0	77.2/18.5
Ceftriaxone	0.12	>8	75.1/23.5	75.1/23.5
Gentamicin	≤1	>8	88.4/11.1	86.5/11.6
Meropenem	0.03	0.12	95.6/3.9	96.1/2.0
Piperacillin-tazobactam	2	>64	85.3/10.4	80.9/14.7
Tigecycline	0.12	1	99.7/0.0[d]	95.9/0.3
Pseudomonas aeruginosa (100)				
Delafloxacin	0.25	>4	-	-
Ciprofloxacin	0.25	>4	74.0/20.0	66.0/26.0
Levofloxacin	0.5	>4	70.0/23.0	62.0/30.0
Amikacin	2	16	91.0/4.0	84.0/9.0
Aztreonam	8	>16	53.0/33.0	1.0/33.0
Cefepime	4	>16	80.0/12.0	80.0/20.0
Ceftazidime	4	>32	74.0/18.0	74.0/26.0
Colistin	2	2	99.0/0.0	100.0/0.0
Gentamicin	≤1	>8	81.0/14.0	81.0/19.0
Meropenem	1	16	70.0/20.0	70.0/11.0
Piperacillin-tazobactam	8	>64	74.0/18.0	74.0/26.0

Antimicrobial agent	MIC_{50}	MIC_{90}	CLSI[a] %S / %R	EUCAST[a] %S / %R
Acinetobacter baumannii-calcoaceticus species complex (100)				
Delafloxacin	4	>4	-	-
Ciprofloxacin	>4	>4	17.0/83.0	17.0/83.0
Levofloxacin	>4	>4	18.0/66.0	17.0/82.0
Amikacin	>32	>32	29.0/66.0	27.0/71.0
Ampicillin-sulbactam	32	>32	25.0/65.0	-
Cefepime	>16	>16	21.0/75.0	-
Ceftazidime	>32	>32	18.0/78.0	-
Colistin	1	2	90.0/10.0	90.0/10.0
Gentamicin	>8	>8	33.0/64.0	33.0/67.0
Meropenem	32	>32	30.3/65.7	30.3/64.6
Piperacillin-tazobactam	>64	>64	18.2/72.7	-

a. Criteria as published by CLSI [2015] and EUCAST [2015]
b. Organisms include: *Citrobacter braakii* (4), *C. freundii* (22), *C. freundii* species complex (11), *C. koseri* (23), *Enterobacter aerogenes* (21), *E. amnigenus* (2), *E. asburiae* (3), *Escherichia coli* (200), *E. cloacae* (58), *E. cloacae* species complex (10), *E. kobei* (1), *Hafnia alvei* (2), *Kluyvera ascorbata* (1), *Klebsiella oxytoca* (36), *K. pneumoniae* (164), *Morganella morganii* (38), *Proteus hauseri* (1), *P. mirabilis* (57), *P. penneri* (1), *P. vulgaris* (15), *Providencia rettgeri* (7), *P. stuartii* (6), Unspeciated *Raoultella* (4), *Raoultella ornithinolytica* (1), *R. planticola* (1), *Serratia liquefaciens* (3), *S. marcescens* (56), *S. rubidaea* (1), *S. odorifera* (1)
c. Intermediate interpreted as SDD
d. Breakpoints from FDA Package Insert revised 12/2014