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In Vitro Profiling of Ceftaroline against a Collection of Recent Bacterial Clinical Isolates from across the United States▽

Yigong Ge,[1] Donald Biek,[1]* George H. Talbot,[1]† and Daniel F. Sahm[2]

Cerexa, Inc., Alameda, California,[1] and Eurofins Medinet, Herndon, Virginia[2]

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This study evaluated the in vitro activity of ceftaroline, a novel cephalosporin with broad-spectrum activity against gram-negative and -positive pathogens, against 4,151 recent clinical isolates collected in the United States. Ceftaroline was very potent against bacteria found in community- and hospital-acquired infections, including methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *Streptococcus pneumoniae*, and common *Enterobacteriaceae* spp.

Antimicrobial resistance is an escalating problem in both nosocomial and community-acquired bacterial infections (3, 12, 13). Pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) are becoming more virulent and are increasingly found in community-acquired infections, particularly in skin and soft-tissue infections (1, 17, 18). The development of resistance to vancomycin and newer classes of antibiotics active against MRSA, such as linezolid and daptomycin, is worrisome (14, 24, 26). The prevalence of drug-resistant (including β-lactam-resistant) *Streptococcus pneumoniae* has increased in the United States during recent years (4, 5, 10). In addition, resistance is common among gram-negative bacteria, some of which produce β-lactamases (including extended-spectrum β-lactamases [ESBL]) and/or exhibit increased efflux activity (12, 19, 22). There is a clinical need for new antibiotics that are active against multidrug-resistant gram-positive and gram-negative pathogens (25, 27).

Ceftaroline fosamil (formerly PPI-0903, TAK-599) is a novel, parenteral, cephalosporin prodrug that is converted in vivo to the microbiologically active form, ceftaroline. Ceftaroline has broad-spectrum activity that encompasses many community- and hospital-acquired pathogens, including MRSA, multidrug-resistant *S. pneumoniae* (MDRSP), and common (non-ESBL-producing) gram-negative bacteria (11, 15, 23). This study evaluated the in vitro activity of ceftaroline against a collection of recent clinical isolates from the United States, including bacteria exhibiting resistance to currently available antimicrobial agents.

(A preliminary report of these results was presented at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy in Chicago, IL, 17 to 20 September 2007.)

A total of 4,151 clinical isolates collected primarily between 2004 and 2006 at hospitals throughout the United States were analyzed. Exceptions included *Providencia* spp., collected from 2001 to 2002, and *Pasteurella multocida*, isolated from Luxembourg. Thirteen *S. aureus* isolates were collected before 2004, 7 of which were collected outside the United States. After being identified at a local laboratory, isolates were shipped on Copan Amies agar gel transport swabs (Copan, Brescia, Italy) to a central laboratory (Eurofins Medinet, Herndon, VA) for confirmatory identification and susceptibility testing. Confirmatory identification was accomplished using routine microbiologic methodologies in accordance with those of Murray (20) and included the use of an automated identification system (Vitek; bioMérieux, Durham, NC) as appropriate. All isolates were tested for their susceptibilities to ceftaroline and appropriate comparator antimicrobial agents as shown in Tables 1 and 2.

Antimicrobial susceptibility testing by broth microdilution adhered to CLSI guidelines M7-A7, employing commercially prepared frozen panels (TREK Diagnostic Systems, Cleveland, OH) (8). Susceptibility interpretative criteria for comparator antibiotics were adopted from CLSI documents M100-S16 and M45-A (7, 9). Quality control was monitored by using the following organisms: *Escherichia coli* ATCC 25922 and ATCC 35218, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, *S. aureus* ATCC 29213, *Haemophilus influenzae* ATCC 49247 and ATCC 49766, and *S. pneumoniae* ATCC 49619. Ceftaroline (PPI-0903 M; lot no. M599-R1001) was provided by Cerexa, Inc., and other comparators were purchased from appropriate commercial sources.

The in vitro activity of ceftaroline in comparison to the activities of selected antimicrobial agents against gram-positive pathogens is summarized in Table 1. Ceftaroline was highly active in vitro against gram-positive bacteria, including resistant isolates, and had lower MICs than ceftazidime and ceftriaxone against all strains tested. Ceftaroline had an MIC at which 90% of isolates were inhibited (MIC_{90}) of 0.25 μg/ml for methicillin-susceptible *S. aureus* (MSSA) compared with 4 μg/ml for ceftriaxone, 1 μg/ml for vancomycin, and ≤0.12 μg/ml for imipenem. Ceftaroline had potent activity in vitro against methicillin-resistant strains (MIC_{90} = 1 μg/ml), and all MRSA isolates were inhibited at an MIC of 2 μg/ml or less. Ceftaroline was the most active β-lactam antibiotic tested against MRSA. Ceftaroline also exhibited potent activity in vitro against coagulase-negative staphylococci, with an MIC_{90} of 0.12 μg/ml for oxacillin-susceptible isolates and an MIC of 0.5 μg/ml for oxacillin-resistant isolates.

* Corresponding author. Mailing address: Cerexa, Inc., 1751 Harbor Bay Parkway, Alameda, California. Phone: (510) 747-3956. Fax: (510) 747-3940. E-mail: dbiek@cerexa.com.

† Present address: Talbot Advisors, LLC, Maplewood Avenue, Wayne, Pennsylvania.

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TABLE 1. Antimicrobial susceptibility of ceftaroline and selected comparator antimicrobial agents against gram-positive organisms[b]

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Staphylococcus aureus						
MSSA (348)						
Ceftaroline	0.25	0.25	≤0.03–1	NA	NA	NA
Ceftazidime	8	8	2–>32	92	6.3	1.7
Ceftriaxone	2	4	1–>32	97.1	2.6	0.3
Daptomycin	0.25	0.5	≤0.12–2	99.4	NA	NA
Erythromycin	0.5	>8	≤0.12–>8	65.2	2.3	32.5
Imipenem	≤0.12	≤0.12	≤0.12–16	99.7	0	0.3
Levofloxacin	0.12	16	0.06–>16	83.9	0.9	15.2
Linezolid	2	2	≤0.5–4	100	NA	NA
Oxacillin	0.25	0.5	≤0.06–2	100	NA	0
Penicillin	4	>16	≤0.12–>16	16.7	NA	83.3
Vancomycin	0.5	1	≤0.25–4	98.3	1.7	0
MRSA (661)						
Ceftaroline	0.5	1	0.12–2	NA	NA	NA
Ceftazidime	32	>32	2–>32	11	34.9	54
Ceftriaxone	16	>32	0.5–>32	14.2	52.6	33.1
Daptomycin	0.25	0.5	≤0.12–2	99.2	NA	NA
Erythromycin	>8	>8	0.25–>8	4.5	1.1	94.4
Imipenem	0.25	>16	≤0.12–>16	84.6	2	13.5
Levofloxacin	8	>16	0.12–>16	25.6	1.2	73.2
Linezolid	2	2	≤0.5–4	100	NA	NA
Oxacillin	>8	>8	4–>8	0	NA	100
Penicillin	>16	>16	≤0.12–>16	0.5	NA	99.5
Vancomycin	1	1	≤0.25–>16	97.9	1.8	0.3
CNS						
OXA-S (201)						
Ceftaroline	0.06	0.12	≤0.03–0.5	NA	NA	NA
Ceftazidime	4	8	≤1–32	93.5	6	0.5
Ceftriaxone	1	4	≤0.25–16	98	2	0
Daptomycin	0.25	0.5	≤0.12–1	100	NA	NA
Erythromycin	1	>8	≤0.12–>8	49.8	1	49.3
Imipenem	≤0.12	≤0.12	≤0.12–0.5	100	0	0
Levofloxacin	0.12	8	≤0.03–>16	81.6	0.5	17.9
Linezolid	1	2	≤0.5–4	100	NA	NA
Oxacillin	0.12	0.25	≤0.06–0.25	100	NA	0
Penicillin	0.5	2	≤0.12–>16	32.3	NA	67.7
Vancomycin	1	2	≤0.25–2	100	0	0
OXA-R (299)						
Ceftaroline	0.5	0.5	0.06–2	NA	NA	NA
Ceftazidime	32	>32	4–>32	10	23.7	66.2
Ceftriaxone	16	>32	1–>32	27.1	50.8	22.1
Daptomycin	0.5	0.5	≤0.12–2	99.7	NA	NA
Erythromycin	>8	>8	≤0.12–>8	18.4	0.3	81.3
Imipenem	0.5	16	≤0.12–>16	77.3	6.4	16.4
Levofloxacin	8	>16	0.12–>16	21.7	4.3	73.9
Linezolid	1	2	≤0.5–>8	99.3	NA	NA
Oxacillin	>8	>8	0.5–>8	0	NA	100
Penicillin	8	>16	≤0.12–>16	2.3	NA	97.7
Vancomycin	1	2	0.5–2	100	0	0
Streptococcus pneumoniae						
PEN-S (202)						
Ceftaroline	≤0.008	0.015	≤0.008–0.12	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–16	NA	NA	NA
Ceftriaxone	0.03	0.06	≤0.015–1	100	0	0
Daptomycin	0.06	0.12	≤0.03–0.5	NA	NA	NA
Erythromycin	0.03	0.5	≤0.015–>16	89.1	1	9.9
Imipenem	≤0.015	≤0.015	≤0.015–1	96.5	3	0.5
Levofloxacin	0.5	1	0.25–8	98.5	0	1.5

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TABLE 1—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Linezolid	1	1	≤0.25–2	100	NA	NA
Vancomycin	0.25	0.5	≤0.06–1	100	NA	NA
PEN-I (103)						
Ceftaroline	0.015	0.06	≤0.008–0.5	NA	NA	NA
Ceftazidime	2	8	≤1–>32	NA	NA	NA
Ceftriaxone	0.12	0.5	≤0.015–8	97.1	1.9	1
Daptomycin	0.06	0.12	≤0.03–0.25	NA	NA	NA
Erythromycin	2	>16	≤0.015–>16	48.5	0	51.5
Imipenem	0.03	0.25	≤0.015–1	88.3	10.7	1
Levofloxacin	0.5	1	0.25–>8	97.1	0	2.9
Linezolid	1	1	0.5–2	100	NA	NA
Vancomycin	0.25	0.5	0.12–0.5	100	NA	NA
PEN-R (296)						
Ceftaroline	0.12	0.12	≤0.008–0.5	NA	NA	NA
Ceftazidime	16	32	≤1–>32	NA	NA	NA
Ceftriaxone	1	2	≤0.015–8	79.4	13.9	6.8
Daptomycin	0.06	0.12	≤0.03–0.25	NA	NA	NA
Erythromycin	8	>16	≤0.015–>16	28.4	0	71.6
Imipenem	0.25	1	≤0.015–4	12.5	76.7	10.8
Levofloxacin	0.5	1	0.12–8	99.3	0	0.7
Linezolid	1	1	0.5–2	100	NA	NA
Vancomycin	0.25	0.5	0.12–0.5	100	NA	NA
Streptococcus pyogenes						
ERY-S (91)						
Ceftaroline	≤0.008	≤0.008	≤0.008–0.03	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–4	NA	NA	NA
Ceftriaxone	≤0.015	0.03	≤0.015–0.5	100	NA	NA
Daptomycin	≤0.03	0.06	≤0.03–0.5	100	NA	NA
Erythromycin	0.03	0.06	≤0.015–0.25	100	0	0
Imipenem	≤0.015	≤0.015	≤0.015–0.06	NA	NA	NA
Levofloxacin	0.5	1	0.03–2	100	0	0
Linezolid	1	1	0.5–2	100	NA	NA
Penicillin	≤0.12	≤0.12	≤0.12–0.25	98.9	NA	NA
Vancomycin	0.25	0.5	0.25–1	100	NA	NA
ERY-NS (10)						
Ceftaroline	≤0.008	0.015	≤0.008–0.03	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–4	NA	NA	NA
Ceftriaxone	0.03	0.12	≤0.015–0.25	100	NA	NA
Daptomycin	≤0.03	0.25	≤0.03–0.25	100	NA	NA
Erythromycin	8	>16	0.5–>16	0	20	80
Imipenem	≤0.015	≤0.015	≤0.015–0.06	NA	NA	NA
Levofloxacin	0.5	1	0.25–1	100	0	0
Linezolid	1	1	1–1	100	NA	NA
Penicillin	≤0.12	≤0.12	≤0.12–≤0.12	100	NA	NA
Vancomycin	0.25	0.5	0.25–1	100	NA	NA
Streptococcus agalactiae						
ERY-S (59)						
Ceftaroline	0.015	0.015	≤0.008–0.06	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–2	NA	NA	NA
Ceftriaxone	0.06	0.12	0.03–0.25	100	NA	NA
Daptomycin	0.12	0.12	≤0.03–0.25	100	NA	NA
Erythromycin	0.03	0.06	≤0.015–0.06	100	NA	NA
Imipenem	≤0.015	0.03	≤0.015–0.03	NA	NA	NA
Levofloxacin	0.5	1	0.12–2	100	0	0
Linezolid	1	1	1–1	100	NA	NA
Penicillin	≤0.12	≤0.12	≤0.12–≤0.12	100	NA	NA
Vancomycin	0.5	0.5	0.25–0.5	100	NA	NA

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TABLE 1—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
ERY-NS (42)						
Ceftaroline	0.015	0.015	≤0.008–0.12	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–8	NA	NA	NA
Ceftriaxone	0.06	0.12	0.03–1	97.6	NA	NA
Daptomycin	0.12	0.25	0.06–0.5	100	NA	NA
Erythromycin	16	>16	0.5–>16	0	7.1	92.9
Imipenem	≤0.015	0.03	≤0.015–0.06	NA	NA	NA
Levofloxacin	1	1	0.5–>8	97.6	0	2.4
Linezolid	1	1	0.5–1	100	NA	NA
Penicillin	≤0.12	≤0.12	≤0.12–2	95.2	NA	NA
Vancomycin	0.5	0.5	≤0.06–1	100	NA	NA
Viridans streptococci						
PEN-S (87)						
Ceftaroline	≤0.008	0.03	≤0.008–0.03	NA	NA	NA
Ceftazidime	≤1	4	≤1–8	NA	NA	NA
Ceftriaxone	0.06	0.25	≤0.015–0.5	100	0	0
Daptomycin	0.25	0.5	≤0.03–1	100	NA	NA
Erythromycin	0.06	4	≤0.015–>16	58.6	1.1	40.2
Imipenem	≤0.015	0.06	≤0.015–0.12	NA	NA	NA
Levofloxacin	1	1	≤0.015–2	100	0	0
Linezolid	1	1	≤0.25–1	100	0	0
Penicillin	≤0.12	≤0.12	≤0.12–≤0.12	100	0	0
Vancomycin	0.5	0.5	≤0.06–1	100	NA	NA
PEN-NS (14)						
Ceftaroline	0.12	0.5	0.015–1	NA	NA	NA
Ceftazidime	8	>32	≤1–>32	NA	NA	NA
Ceftriaxone	2	8	0.06–>16	28.6	42.9	28.6
Daptomycin	0.25	0.5	0.12–1	100	0	0
Erythromycin	2	>16	0.12–>16	21.4	7.1	71.4
Imipenem	0.06	1	≤0.015–4	NA	NA	NA
Levofloxacin	1	2	0.12–>8	92.9	0	7.1
Linezolid	1	1	0.5–1	100	0	0
Penicillin	0.5	8	0.25–8	0	71.4	28.6
Vancomycin	0.5	1	0.5–2	92.9	NA	NA
Enterococcus faecalis						
VAN-S (157)						
Ceftaroline	2	4	0.5–8	NA	NA	NA
Ceftazidime	>32	>32	>32–>32	NA	NA	NA
Ceftriaxone	>32	>32	8–>32	NA	NA	NA
Daptomycin	1	1	0.25–4	100	0	0
Erythromycin	>8	>8	≤0.12–>8	10.2	29.9	59.9
Imipenem	1	2	0.25–4	NA	NA	NA
Levofloxacin	1	>16	0.5–>16	59.2	0	40.8
Linezolid	2	2	1–2	100	0	0
Oxacillin	>8	>8	2–>8	NA	NA	NA
Penicillin	2	4	1–8	100	0	0
Vancomycin	1	2	0.5–2	100	0	0
VAN-R (25)						
Ceftaroline	4	4	1–8	NA	NA	NA
Ceftazidime	>32	>32	4–>32	NA	NA	NA
Ceftriaxone	>32	>32	1–>32	NA	NA	NA
Daptomycin	0.5	1	0.25–1	100	0	0
Erythromycin	>8	>8	1–>8	0	4	96
Imipenem	1	2	0.25–2	NA	NA	NA
Levofloxacin	>16	>16	1–>16	4	0	96
Linezolid	2	2	1–2	100	0	0
Oxacillin	>8	>8	2–>8	NA	NA	NA
Penicillin	2	4	1–8	100	0	0
Vancomycin	>16	>16	>16–>16	0	0	100

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TABLE 1—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Enterococcus faecium						
VAN-R (26)						
Ceftaroline	>16	>16	4–>16	NA	NA	NA
Ceftazidime	>32	>32	>32–>32	NA	NA	NA
Ceftriaxone	>32	>32	>32–>32	NA	NA	NA
Daptomycin	2	4	0.5–4	100	0	0
Erythromycin	>8	>8	2–>8	0	7.7	92.3
Imipenem	>16	>16	>16–>16	NA	NA	NA
Levofloxacin	>16	>16	>16–>16	0	0	100
Linezolid	2	2	1–2	100	0	0
Oxacillin	>8	>8	>8–>8	NA	NA	NA
Penicillin	>16	>16	>16–>16	0	0	100
Vancomycin	>16	>16	>16–>16	0	0	100

[a] MICs reported only for categories composed of 10 or more isolates.
[b] CNS, coagulase-negative staphylococci; ERY, erythromycin; I, intermediate; NS, nonsusceptible; OXA, oxacillin; PEN, penicillin; R, resistant; S, susceptible; VAN, vancomycin; NA, not available (CLSI breakpoints unavailable for interpretation of susceptible, intermediate, or resistant isolates).

Ceftaroline exhibited high in vitro activity against all strains of streptococci tested. As with other β-lactams, MIC_{90}s were lower against penicillin-susceptible strains of *S. pneumoniae* (MIC_{90} = 0.015 μg/ml) than against penicillin-resistant strains (MIC_{90} = 0.12 μg/ml), although ceftaroline remained highly active regardless of penicillin-susceptibility status ($MIC_{90} \leq$ 0.5 μg/ml). Ceftaroline was very potent against beta-hemolytic streptococci, *Streptococcus pyogenes* and *Streptococcus agalactiae*, and its activity was not affected by the macrolide-susceptibility status of the strains tested. The highest ceftaroline MICs for any isolate were 0.03 μg/ml for *S. pyogenes* and 0.12 μg/ml for *S. agalactiae*. Viridans group streptococci were susceptible to ceftaroline with an MIC_{90} of 0.03 μg/ml for penicillin-susceptible strains and 0.5 μg/ml for penicillin-resistant strains. Against *E. faecalis*, ceftaroline had an MIC_{90} of 4 μg/ml, and activity was not affected by the vancomycin-susceptibility status of the strains tested. Similarly to other β-lactam agents, ceftaroline exhibited minimal activity against *Enterococcus faecium*.

As shown in Table 2, the spectrum of activity of ceftaroline for *Enterobacteriaceae* spp. was similar to that of other extended-spectrum cephalosporins, including ceftazidime and ceftriaxone. The MIC_{90} of 1 μg/ml for ceftaroline against the collection of cephalosporin-susceptible *Enterobacteriaceae* isolates was slightly higher than that for ceftazidime (0.5 μg/ml) and ceftriaxone (0.25 μg/ml). With regard to individual species of *Enterobacteriaceae*, ceftaroline exhibited similar activity to that of ceftazidime and ceftriaxone among cephalosporin-susceptible populations of *E. coli*, *Citrobacter freundii*, *Enterobacter cloacae*, and *Klebsiella pneumoniae*. As shown in Table 2, ceftaroline MIC_{90}s were considerably higher relative to cefepime, ceftazidime, and ceftriaxone against *Proteus mirabilis*, *Morganella morganii*, *Serratia marcescens*, and *Providencia* spp. Similarly to third-generation cephalosporins, ceftaroline was not active against ceftazidime-nonsusceptible *Enterobacteriaceae* spp., which included ESBL-producing or AmpC-overexpressing strains. The MIC_{90} of ceftaroline was >16 μg/ml for imipenem-susceptible and multidrug-resistant strains of *Acinetobacter*, mainly *Acinetobacter baumannii*, which was similar to that for ceftriaxone and levofloxacin.

Ceftaroline had potent activity in vitro against *H. influenzae*, regardless of the production of β-lactamase. Ceftaroline also exhibited potent activity against all isolates of *Moraxella catarrhalis*, regardless of the presence of β-lactamases (93 of the 102 strains were β-lactamase positive) (data not shown), demonstrating the stability of ceftaroline to β-lactamases associated with this pathogen. Additionally, ceftaroline was very active in vitro against *P. multocida*.

Ceftaroline demonstrated potent in vitro activity against a wide spectrum of clinically relevant organisms, with MICs that were either lower than or similar to those of other cephalosporins. Ceftaroline was particularly active against *S. aureus* and beta-hemolytic streptococci, gram-positive bacteria commonly associated with skin and wound infections. Ceftaroline exhibited low MIC ranges for *S. aureus*, extending from ≤0.03 to 1 μg/ml for MSSA and 0.12 to 2 μg/ml for MRSA, which set this agent apart from currently available β-lactams. Because MRSA is becoming increasingly prevalent in hospital- and community-acquired infections (1, 18), the availability of a new cephalosporin with bactericidal activity against MRSA would have significant favorable clinical implications (16).

Ceftaroline was highly active against *S. pneumoniae* as well as β-lactamase-positive and -negative isolates of *H. influenzae* and *M. catarrhalis*, pathogens frequently associated with respiratory tract infections (2). There is increasing evidence that *S. pneumoniae*, one of the most common causes of community-acquired pneumonia, is developing resistance to many of the currently available antibiotics, including macrolides, quinolones, and older cephalosporins (6, 21). In this evaluation, ceftaroline was highly active against *S. pneumoniae*, regardless of penicillin-susceptibility status. In addition, ceftaroline maintained activity against many common gram-negative pathogens similar to that of other third-generation cephalosporins, a spectrum of activity that differentiates it from many newer antibiotics that are active only against gram-positive organisms.

In conclusion, ceftaroline exhibited potent in vitro activity against a broad collection of recent gram-positive and gram-negative bacterial isolates from hospitals throughout the United States. This in vitro profile suggests that ceftaroline has

TABLE 2. Antimicrobial susceptibility of ceftaroline and selected comparator antimicrobial agents against gram-negative organisms[b]

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Enterobacteriaceae						
CAZ-S (833)						
Ceftaroline	0.06	1	≤0.03–>16	NA	NA	NA
Ampicillin	32	>32	≤0.25–>32	35.2	7.8	57
Cefepime	≤0.03	0.12	≤0.03–>32	98.8	0.2	1
Ceftazidime	0.12	0.5	≤0.03–8	100	0	0
Ceftriaxone	≤0.06	0.25	≤0.06–>16	98	2	0
Gentamicin	0.5	2	≤0.12–>16	92.6	1.6	5.9
Imipenem	0.25	1	≤0.06–4	100	0	0
Levofloxacin	0.06	4	≤0.03–>16	89.6	1.1	9.4
Piperacillin/tazobactam	2	4	≤0.5–>64	97	1.4	1.6
CAZ-NS (220)						
Ceftaroline	>16	>16	0.12–>16	NA	NA	NA
Ampicillin	>32	>32	32–>32	0	0	100
Cefepime	2	>32	≤0.03–>32	71.4	5.5	23.2
Ceftazidime	>32	>32	16–>32	0	10	90
Ceftriaxone	>16	>16	≤0.06–>16	13.2	86.8	0
Gentamicin	4	>16	≤0.12–>16	52.3	7.3	40.5
Imipenem	0.25	4	≤0.06–>32	92.3	3.2	4.5
Levofloxacin	8	>16	≤0.03–>16	41.8	6.8	51.4
Piperacillin/tazobactam	32	>64	≤0.5–>64	43.2	18.2	38.6
Citrobacter freundii						
CAZ-S (50)						
Ceftaroline	0.12	0.25	0.06–16	NA	NA	NA
Ampicillin	16	>32	4–>32	36	22	42
Cefepime	≤0.03	0.12	≤0.03–0.12	100	0	0
Ceftazidime	0.25	1	0.12–8	100	0	0
Ceftriaxone	0.12	0.5	≤0.06–1	100	0	0
Gentamicin	0.5	8	0.25–>16	88	2	10
Imipenem	0.5	1	0.12–1	100	0	0
Levofloxacin	≤0.03	1	≤0.03–4	98	2	0
Piperacillin/tazobactam	2	4	1–8	100	0	0
CAZ-NS (33)						
Ceftaroline	>16	>16	4–>16	NA	NA	NA
Ampicillin	>32	>32	>32–>32	0	0	100
Cefepime	1	4	0.12–8	100	0	0
Ceftazidime	>32	>32	16–>32	0	3	97
Ceftriaxone	>16	>16	4–>16	6.1	93.9	0
Gentamicin	0.5	16	0.25–>16	81.8	0	18.2
Imipenem	0.5	1	0.12–2	100	0	0
Levofloxacin	0.25	16	≤0.03–>16	72.7	3	24.2
Piperacillin/tazobactam	32	>64	2–>64	24.2	36.4	39.4
Enterobacter cloacae						
CAZ-S (50)						
Ceftaroline	0.12	1	≤0.03–>16	NA	NA	NA
Ampicillin	32	>32	0.5–>32	20	14	66
Cefepime	0.06	0.12	≤0.03–16	98	2	0
Ceftazidime	0.25	1	0.06–8	100	0	0
Ceftriaxone	0.12	1	≤0.06–>16	98	2	0
Gentamicin	0.25	0.5	≤0.12–>16	96	2	2
Imipenem	0.5	0.5	0.12–2	100	0	0
Levofloxacin	≤0.03	0.5	≤0.03–16	94	4	2
Piperacillin/tazobactam	2	4	≤0.5–>64	98	0	2
CAZ-NS (35)						
Ceftaroline	>16	>16	0.12–>16	NA	NA	NA
Ampicillin	>32	>32	32–>32	0	0	100
Cefepime	1	4	0.12–16	97.1	2.9	0
Ceftazidime	>32	>32	16–>32	0	8.6	91.4
Ceftriaxone	>16	>16	1–>16	8.6	91.4	0

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TABLE 2—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Gentamicin	0.5	>16	≤0.12–>16	71.4	11.4	17.1
Imipenem	0.25	1	0.12–>32	97.1	0	2.9
Levofloxacin	0.12	16	≤0.03–>16	62.9	11.4	25.7
Piperacillin/tazobactam	>64	>64	1–>64	25.7	20	54.3
Escherichia coli						
CAZ-S (345)						
Ceftaroline	0.06	0.5	≤0.03–>16	NA	NA	NA
Ampicillin	4	>32	≤0.25–>32	58.3	0.9	40.9
Cefepime	≤0.03	0.12	≤0.03–>32	98.3	0	1.7
Ceftazidime	0.12	0.25	≤0.03–8	100	0	0
Ceftriaxone	≤0.06	0.12	≤0.06–>16	97.4	2.6	0
Gentamicin	0.5	2	≤0.12–>16	91.9	0.6	7.5
Imipenem	0.12	0.25	≤0.06–1	100	0	0
Levofloxacin	≤0.03	16	≤0.03–>16	86.4	0	13.6
Piperacillin/tazobactam	1	4	≤0.5–>64	96.5	1.2	2.3
CAZ-NS (63)						
Ceftaroline	>16	>16	2–>16	NA	NA	NA
Ampicillin	>32	>32	>32–>32	0	0	100
Cefepime	2	>32	0.25–>32	57.1	7.9	34.9
Ceftazidime	>32	>32	16–>32	0	12.7	87.3
Ceftriaxone	>16	>16	1–>16	9.5	90.5	0
Gentamicin	16	>16	0.5–>16	46	3.2	50.8
Imipenem	0.25	1	≤0.06–>32	96.8	0	3.2
Levofloxacin	>16	>16	≤0.03–>16	14.3	0	85.7
Piperacillin/tazobactam	16	>64	2–>64	68.3	14.3	17.5
Klebsiella pneumoniae						
CAZ-S (210)						
Ceftaroline	0.06	0.25	≤0.03–>16	NA	NA	NA
Ampicillin	>32	>32	1–>32	5.2	14.8	80
Cefepime	≤0.03	0.12	≤0.03–0.5	100	0	0
Ceftazidime	0.12	0.25	≤0.03–8	100	0	0
Ceftriaxone	≤0.06	0.12	≤0.06–16	99.5	0.5	0
Gentamicin	0.25	0.5	≤0.12–>16	97.1	1	1.9
Imipenem	0.12	0.5	0.12–2	100	0	0
Levofloxacin	0.06	0.25	≤0.03–>16	98.1	0.5	1.4
Piperacillin/tazobactam	2	8	≤0.5–>64	97.1	2.4	0.5
CAZ-NS (66)						
Ceftaroline	>16	>16	1–>16	NA	NA	NA
Ampicillin	>32	>32	32–>32	0	0	100
Cefepime	8	>32	≤0.03–>32	57.6	7.6	34.8
Ceftazidime	>32	>32	16–>32	0	1.5	98.5
Ceftriaxone	>16	>16	≤0.06–>16	12.1	87.9	0
Gentamicin	8	>16	≤0.12–>16	43.9	12.1	43.9
Imipenem	0.12	16	≤0.06–>32	80.3	9.1	10.6
Levofloxacin	8	>16	≤0.03–>16	37.9	7.6	54.5
Piperacillin/tazobactam	>64	>64	≤0.5–>64	24.2	13.6	62.1
Morganella morganii						
CAZ-S (34)						
Ceftaroline	0.06	16	≤0.03–>16	NA	NA	NA
Ampicillin	>32	>32	1–>32	8.8	5.9	85.3
Cefepime	≤0.03	0.06	≤0.03–0.06	100	0	0
Ceftazidime	0.06	4	≤0.03–8	100	0	0
Ceftriaxone	≤0.06	1	≤0.06–4	100	0	0
Gentamicin	0.5	4	0.25–>16	91.2	0	8.8
Imipenem	2	2	0.25–4	100	0	0
Levofloxacin	≤0.03	8	≤0.03–>16	76.5	2.9	20.6
Piperacillin/tazobactam	≤0.5	1	≤0.5–4	100	0	0

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TABLE 2—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Proteus mirabilis						
CAZ-S (58)						
Ceftaroline	0.06	4	≤0.03–>16	NA	NA	NA
Ampicillin	1	>32	0.5–>32	72.4	0	27.6
Cefepime	0.06	0.5	≤0.03–16	98.3	1.7	0
Ceftazidime	0.06	0.12	≤0.03–4	100	0	0
Ceftriaxone	≤0.06	0.12	≤0.06–>16	96.6	3.4	0
Gentamicin	1	8	0.5–>16	84.5	6.9	8.6
Imipenem	2	4	≤0.06–4	100	0	0
Levofloxacin	0.06	16	≤0.03–>16	75.9	3.4	20.7
Piperacillin/tazobactam	≤0.5	1	≤0.5–2	100	0	0
Providencia spp.						
CAZ-S (27)						
Ceftaroline	1	>16	≤0.03–>16	NA	NA	NA
Ampicillin	32	>32	4–>32	22.2	11.1	66.7
Cefepime	0.06	1	≤0.03–4	100	0	0
Ceftazidime	0.25	4	≤0.03–8	100	0	0
Ceftriaxone	≤0.06	2	≤0.06–8	100	0	0
Gentamicin	2	>16	0.25–>16	74.1	11.1	14.8
Imipenem	1	2	0.25–2	100	0	0
Levofloxacin	0.25	>16	≤0.03–>16	66.7	7.4	25.9
Piperacillin/tazobactam	2	16	≤0.5–>64	92.6	3.7	3.7
Serratia marcescens						
CAZ-S (59)						
Ceftaroline	0.5	16	0.12–>16	NA	NA	NA
Ampicillin	>32	>32	8–>32	3.4	13.6	83.1
Cefepime	0.06	0.5	≤0.03–32	96.6	0	3.4
Ceftazidime	0.12	1	≤0.03–8	100	0	0
Ceftriaxone	0.25	4	≤0.06–>16	93.2	6.8	0
Gentamicin	0.5	1	0.25–>16	98.3	0	1.7
Imipenem	0.5	1	0.25–2	100	0	0
Levofloxacin	0.12	1	≤0.03–8	98.3	0	1.7
Piperacillin/tazobactam	2	16	≤0.5–>64	93.2	3.4	3.4
Acinetobacter spp.						
MDR (16)						
Ceftaroline	>16	>16	8–>16	NA	NA	NA
Ampicillin	>32	>32	>32–>32	NA	NA	NA
Cefepime	16	32	4–>32	31.3	31.3	37.5
Ceftazidime	>32	>32	16–>32	0	6.3	93.8
Ceftriaxone	>16	>16	>16–>16	0	100	0
Gentamicin	>16	>16	0.25–>16	18.8	6.3	75
Imipenem	0.5	32	0.25–32	68.8	0	31.3
Levofloxacin	16	>16	2–>16	6.3	6.3	87.5
Piperacillin/tazobactam	>64	>64	32–>64	0	12.5	87.5
IMI-S (47)						
Ceftaroline	4	>16	≤0.03–>16	NA	NA	NA
Ampicillin	16	>32	≤0.25–>32	NA	NA	NA
Cefepime	4	32	0.12–>32	78.7	6.4	14.9
Ceftazidime	4	>32	0.5–>32	63.8	4.3	31.9
Ceftriaxone	16	>16	≤0.06–>16	44.7	55.3	0
Gentamicin	1	>16	≤0.12–>16	74.5	4.3	21.3
Imipenem	0.25	0.5	≤0.06–2	100	0	0
Levofloxacin	0.5	>16	≤0.03–>16	51.1	12.8	36.2
Piperacillin/tazobactam	8	>64	≤0.5–>64	68.1	10.6	21.3
Haemophilus influenzae						
β-lactamase negative (199)						
Ceftaroline	≤0.008	0.015	≤0.008–1	NA	NA	NA
Ampicillin	≤0.25	0.5	≤0.25–16	99	NA	1

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TABLE 2—*Continued*

Bacterium group and antimicrobial agent (no. of isolates tested)	MIC (μg/ml)[a]			% of isolates by category		
	MIC_{50}	MIC_{90}	Range	S	I	R
Cefepime	0.06	0.12	≤0.03–0.5	100	NA	NA
Ceftazidime	0.06	0.12	≤0.03–8	98.5	NA	NA
Ceftriaxone	≤0.06	≤0.06	≤0.06–0.12	100	NA	NA
Gentamicin	1	2	0.25–4	NA	NA	NA
Imipenem	0.25	0.5	≤0.06–1	100	NA	NA
Levofloxacin	0.015	0.03	≤0.004–1	100	NA	NA
Piperacillin/tazobactam	≤0.03	0.06	≤0.03–0.25	100	NA	0
β-lactamase positive (101)						
Ceftaroline	0.015	0.03	≤0.008–2	NA	NA	NA
Ampicillin	32	>32	≤0.25–>32	2	1	97
Cefepime	0.06	0.12	≤0.03–0.5	100	NA	NA
Ceftazidime	0.06	0.12	≤0.03–8	98	NA	NA
Ceftriaxone	≤0.06	≤0.06	≤0.06–0.12	100	NA	NA
Gentamicin	1	2	≤0.12–4	0	NA	NA
Imipenem	0.12	0.5	≤0.06–2	100	NA	NA
Levofloxacin	0.015	0.03	≤0.004–0.03	100	NA	NA
Piperacillin/tazobactam	≤0.03	0.06	≤0.03–2	99	NA	1
Moraxella catarrhalis						
β-lactamase positive (93)						
Ceftaroline	0.06	0.25	≤0.03–0.5	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–≤1	100	NA	NA
Ceftriaxone	≤0.25	1	≤0.25–1	100	NA	NA
Erythromycin	≤0.12	≤0.12	≤0.12–0.25	100	0	0
Imipenem	≤0.12	≤0.12	≤0.12–≤0.12	NA	NA	NA
Levofloxacin	≤0.03	≤0.03	≤0.03–0.06	100	NA	NA
Linezolid	4	4	1–4	NA	NA	NA
Oxacillin	4	>8	≤0.06–>8	NA	NA	NA
Penicillin	4	16	0.25–>16	NA	NA	NA
Pasteurella multocida (22)						
Ceftaroline	≤0.008	0.06	≤0.008–0.06	NA	NA	NA
Ceftazidime	≤1	≤1	≤1–≤1	NA	NA	NA
Ceftriaxone	≤0.015	≤0.015	≤0.015–0.06	100	NA	NA
Erythromycin	2	4	0.25–>16	4.5	18.2	77.3
Imipenem	0.25	2	0.06–4	NA	NA	NA
Levofloxacin	≤0.015	0.03	≤0.015–>8	95.5	NA	NA
Linezolid	4	>4	4–>4	NA	NA	NA
Penicillin	≤0.12	0.25	≤0.12–>8	NA	NA	NA

[a] MICs reported only for categories composed of 10 or more isolates.
[b] CAZ, ceftazidime; IMI, imipenem; MDR, multidrug resistant (defined as concurrent resistance to at least three drugs); NS, nonsusceptible; S, susceptible; NA, not available (CLSI breakpoints unavailable for interpretation of susceptible, intermediate, or resistant isolates).

the potential to become an important addition to the arsenal of currently available antimicrobial therapies as a broad-spectrum antibiotic that may be used in the treatment of both nosocomial and community-acquired infections.

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