Comparative In Vitro Activities of Cefpiramide and Apalcillin Individually and in Combination

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The in vitro activities of cefpiramide and apalcillin were compared with those of other third-generation cephalosporins and extended-spectrum penicillins against over 1,000 clinical bacterial isolates. The activity of cefpiramide against Pseudomonas aeruginosa was comparable to those of piperacillin and cefoperazone, inhibiting 90% of strains at concentrations \leq 16.0 µg/ml. This drug was also active against a broad range of gram-negative organisms but was generally less active than many of the other cephalosporins tested against members of the family Enterobacteriaceae. The activity of cefpiramide against gram-positive organisms was comparable to that of cefoperazone. Apalcillin, along with ceftazidime, was the most active agent tested against P. aeruginosa and Acinetobacter calcoaceticus subsp. anitratus, inhibiting 90% of these strains at concentrations $\leq 8 \mu g/ml$. Against other gram-negative and gram-positive organisms, its activity was similar to that of piperacillin. The activities of both cefpiramide and apalcillin were significantly reduced by the presence of several plasmid-mediated B-lactamases in a series of otherwise isogenic strains of P. aeruginosa in comparison with their activities against a parent strain which lacks these enzymes. Many strains of Enterobacter cloacae were synergistically inhibited by the combination of gentamicin with either cefpiramide (5 of 10 strains) or apalcillin (6 of 10 strains). Most strains of P. aeruginosa were synergistically inhibited by the combination of gentamicin with either cefpiramide (8 of 10 strains) or apalcillin (10 of 10 strains). However, cefoxitin antagonized the activity of both cefpiramide and apalcillin against most of these same strains.

Cefpiramide (SM-1652, WY-44,635) is a new semisynthetic cephalosporin that is structurally related to cefoperazone. A number of recent studies have documented its broad spectrum of activity against both gram-negative and gram-positive organisms. Compared with other cephalosporins, it is particularly active against *Pseudomonas aeruginosa* (6, 8, 14). In addition, cefpiramide has a half-life of approximately 4.5 h in humans, which is significantly longer than those of other third-generation cephalosporins, such as ceftazidime and cefoperazone, but shorter than that of ceftriaxone (10).

Apalcillin (PC-904) is a naphthyridine derivative of ampicillin. Its spectrum of activity is similar to that of piperacillin, although it exhibits greater activity against *P. aeruginosa* than does piperacillin (1, 5, 12, 13). Apalcillin also differs from piperacillin in having a slightly longer half-life and in being largely eliminated by hepatobiliary mechanisms (9).

In the present study, we examined the in vitro activity of both cefpiramide and apalcillin against more than 1,000 routine clinical isolates of gram-positive and gram-negative bacteria as well as organisms selected for resistance to multiple antibiotics. The activity of these two agents was also tested in combination with other β -lactams and gentamicin.

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MATERIALS AND METHODS

Bacterial strains. Gram-negative bacteria used in this study were routine clinical isolates recently collected (1983 to 1984) from the New England Deaconess Hospital and the Massachusetts General Hospital, Boston. The organisms collected were isolated from multiple body sites including urine, sputum, blood, feces, wounds, and cerebrospinal fluid. Duplicate isolates from individual patients were excluded, but otherwise isolates were unselected. β -Lactamase-producing strains of *Neisseria gonorrhoeae* were kindly provided by Clyde Thornsberry (Centers for Disease Control, Atlanta, Ga.).

Routine gram-positive isolates had been collected earlier at the Massachusetts General Hospital. Penicillin-resistant pneumococci and viridans group streptococci were obtained as previously reported (3, 4). In certain specified studies, multiply resistant gram-negative bacilli were used from our collection established over the past 5 to 10 years. The following MIC criteria were used for defining resistance: amikacin, $\geq 32 \mu g/ml$; gentamicin, $\geq 8 \mu g/ml$; carbenicillin, $\geq 32 \mu g/ml$ ($\geq 250 \mu g/ml$ for *P. aeruginosa*); cephalothin, $\geq 32 \mu g/ml$ (11). *P. aeruginosa* transconjugants containing various defined plasmid-mediated β -lactamases were provided by George Jacoby (Massachusetts General Hospital) and have been described previously (2).

Antimicrobial agents. Standard antimicrobial reference powders were obtained from the following sources: apalcillin and cefpiramide, Wyeth Laboratories, Inc., Philadelphia, Pa.; piperacillin, Lederle Laboratories, Pearl River, N.Y.; moxalactam, cefamandole, and cephalothin, Eli Lilly & Co., Indianapolis, Ind.; imipenem and cefoxitin, Merck Sharp & Dohme, Rahway, N.J.; aztreonam, E. R. Squibb & Sons,

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Organism (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (μg/ml)	MIC ₉₀ (μg/ml)
Pseudomonas aeruginosa (90)	Cefpiramide	0.25->128	4	16
	Apalcillin	≤0.06->128	2	8
	Piperacillin	0.5->128	8	16
	Azlocillin	1.0->128	16	32
	Aztreonam	0.25-128	8	32
	Cefoperazone	2.0 -> 128	8	32 > 128
	Cettriaxone	8.0 - > 128	04	>120
	Cefsuladin	1.0->120	8	32
	Gentamicin	0.5->128	4	8
Pseudomonas cepacia (10)	Cefpiramide	1.0->128	65	>128
• • •	Apalcillin	1.0->128	16	>128
	Piperacillin	0.5->128	32	>128
	Aztreonam	2.0->128	64	>128
	Cefoperazone	8.0->128	128	>128
	Ceftriaxone	0.5-32	0.5	16
	Gentaricin	0.5-16 1.0->128	32	>128
Praudomonas fluorascans/putida	Cefniramide	8 0_32	16	16
(10)	Analcillin	2 0-8	4	4
(10)	Piperacillin	2.0-8	8	16
	Aztreonam	32.0-128	64	>128
	Cefoperazone	8.0-64	8	16
	Ceftriaxone	16.0-128	16	128
	Ceftazidime	1.0-16	2	16
	Gentamicin	≤0.06–>128	0.25	1
Pseudomonas maltophilia (20)	Cefpiramide	2.0-128	32	64
	Apalcillin	2.0 - > 128	32	128
	Piperacillin	32.0 - > 128	128	>128
	Aztreonam	8.0 - > 128	120	>120
	Ceftriayone	32.0 - > 128	>128	>128
	Ceftazidime	20 -> 128	> 120	120
	Gentamicin	1.0->128	32	>128
Acinetobacter calcoaceticus subsp.	Cefpiramide	4.0–128	32	64
antiratus (30)	Apalcillin	4.0–16	8	8
	Piperacillin	2.0–>128	16	32
	Aztreonam	8.0–>128	32	64
	Cefoperazone	16.0->128	64	>128
	Ceftriaxone	2.0-64	16	16
	Gentamicin	4.0-32 0.25-64	4	8 2
Aeromonas hydrophila (10)	Cefniramide	1 0-32	2	8
1201011120 11941 0911114 (10)	Apalcillin	2.0-128	4	8
	Piperacillin	1.0–128	2	4
	Aztreonam	≤0.06-0.25	≤0.06	≤0.06
	Cefoperazone	0.25-8	0.5	2
	Ceftriaxone	≤0.06–4	0.5	4
	Ceftazidime	0.125-2	0.25	1
	Gentamicin	0.25–2	0.25	1
Haemophilus influenzae (β-	Cefpiramide	≤0.06-0.5	0.125	0.250
iactamase negative) (20)	Apaicillin	≥0.00-2 <0.0€ 0.5	0.23	0.5
	Aztreonam	≥0.00-0.3 <0.06_0.25	≥0.00 <0.04	U.123 <0.04
	Cefonerazone	<u>0.00_0.25</u> ≤0.06_0.125	<u> </u>	<u>0.00</u> <0.06
	Ceftriaxone	≤0.06	<u></u> ≤0.06	<u></u> ≤0.06
	Ceftazidime	 ≤0.06–0.5	0.125	0.125
	Gentamicin	0.25-8	2	4
Haemophilus influenzae (β-	Cefpiramide	1.0-4	2	2
lactamase positive) (10)	Apalcillin	128.0->128	>128	>128
	Piperacillin	32.0->128	128	>128

TABLE 1. Comparative in vitro activities of cefpiramide and apalcillin

TABLE 1—Continued

Organism (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
	Aztreonam	≤0.06	≤0.06	≤0.06
	Cefoperazone	0.125-0.5	0.125	0.5
	Ceftriaxone	≤0.06	≤0.06	≤0.06
	Ceftazidime	≤0.06-0.125	0.125	0.125
	Gentamicin	2.0-4	2	4
Neisseria gonorrhoeae (β-	Cefpiramide	≤0.06-0.25	≤0.06	0.125
lactamase negative) (10)	Apalcillin	≤0.06-0.5	≤0.06	0.25
	Piperacillin	≤0.06-0.5	≤0.06	≤0.06
	Aztreonam	≤0.06-0.125	≤0.06 <0.06	≤0.06 ≤0.06
	Cettriaxana	≤0.06-0.25 <0.06	≤0.06	≤0.06 <0.06
	Ceftazidime	<0.00	<u>~0.06</u>	0.00 <0.06
	Penicillin	≤0.06-0.125	≤0.06	≤0.06
Neisseria conorrhoeae (B-	Cefniramide	<0.06_0.5	0.25	0.5
lactamase positive) (8)	Apalcillin	1.0-32	2	16
	Piperacillin	0.5-32	1	8
	Aztreonam	≤0.06-0.125	≤0.06	≤0.06
	Cefoperazone	≤0.06-0.25	0.125	0.25
	Ceftriaxone	≤0.06	≤0.06	≤0.06
	Ceftazidime	≤0.06	≤0.06	≤0.06
	Penicillin	1.0-64	8	64
Pasteurella multocida (10)	Cefpiramide	≤0.06–0.125	≤0.06	0.125
	Apalcillin	≤0.06	≤0.06	≤0.06
	Piperacillin	≤0.06-0.125	≤0.06 ≤0.06	0.125
	Aztreonam	≤0.06	≤0.06	≤0.00 0.125
	Ceftriavone	≤0.00 <0.06	≤0.00 <0.06	<0.125
	Ceftazidime	<0.06-0.25	0.125	0.25
	Gentamicin	0.125-1	1	1
Citrobacter diversus (10)	Cefpiramide	0.125-2	0.5	2
	Apalcillin	1.0-8	4	8
	Piperacillin	1.0-8	4	8
	Aztreonam	≤0.06	≤0.06	≤0.06
	Cefoperazone	≤0.06-0.25	≤0.06	0.125
	Ceftriaxone	≤0.06-0.25	≤0.06	≤0.06
	Gentamicin	≤0.06–0.125 ≤0.06–1.0	≤0.06 0.25	≤0.06 0.5
		1.0. 100		× 100
Citrobacter freundii (40)	Cefpiramide	1.0 > 128	4	>128
	Apaicillin	1.0 > 128	2	/120
	Aztreonam	<0.06-64	0 125	32
	Cefoperazone	0.125 > 128	0.5	128
	Ceftriaxone	≤0.06–128	0.125	64
	Ceftazidime	0.125->128	0.5	128
	Gentamicin	0.25-64	0.5	1
Escherichia coli (90)	Cefpiramide	0.125->128	1	32
× ,	Apalcillin	0.5->128	1	128
	Piperacillin	0.5->128	2	128
	Aztreonam	≤0.06-0.25	≤0.06	0.125
	Cefoperazone	≤0.06-32	0.25	4
	Ceftriaxone	≤0.06 ~0.06 0.5	≤0.06 0.125	≤0.06 0.25
	Gentamicin	<u>≤0.06–0.5</u> 0.25–2	0.125	1
Enterobactor con (00)	Cafniramida	በ ንና_>1ንዩ	4	128
Emerodacier spp. (90)	Analcillin	0.5 > 120	4	64
	Piperacillin	0.25->128	4	32
	Aztreonam	≤0.06–64	≤0.06	16
	Cefoperazone	≤0.06–>128	0.5	16
	Ceftriaxone	≤0.06->128	0.125	16
	Ceftazidime	≤0.06-128	0.25	32
	Gentamicin	0.25–1	0.5	0.5

TABLE 1-Continued

Klebsiella avyoca (30) Cefpiranide Apaleilln 1.0->128 8 32 Araconan -0.06-2 -0.06 0.5 Atteonan -0.06-2 -0.06 0.5 Cefoperazone 0.125-312 2 -0.06 0.5 Cefoperazone 0.125-312 2 -0.06 0.5 Cefoperazone 0.125-512 0.5 0.125 0.5 Klebsiella pneumoniae (60) Cefpiranide 0.125-64 2 16 Apaleilln 0.5-64 8 16 16 Piperaellin 10-64 8 16 16 Apaleilln 0.25-64 8 16 16 Piperaellin 0.06-1 =0.06-3 1 16 Ceftrazidine 50.0-64 0.25 4 6 12 Ceftrazidine 8.0-2128 16 12 2 16 Ceftrazidine 0.05-11 =0.06 =0.06 0.05 1 Ceftrazidine =0.06-16 =0.06<	Organism (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
Apslellin 4.0~2128 8 16 Prepencillin 1.0~2128 50 0.0 0.1 Artroname 50.06-3 50 0.125 0.125 Certuzidime 50.06-0.5 0.125 0.125 0.125 Gentamicin 0.25-1 0.5 0.5 0.5 Klebsiella pneumoniae (60) Cefpiramide 0.125-64 2 16 Apaleillin 0.5-64 8 15 0.6 20.06 Apaleillin 0.5-64 8 16 32 0.6 20.05 <	Klebsiella oxytoca (30)	Cefpiramide	1.0->128	8	32
Piperacilin Arteronam 1.0->128 8 32 Actronam 0.05 200 0.3 Ceftoperazone 0.125-313 2 4 Ceftoperazone 0.125-313 2 0.05 Ceftorazione 0.25-1 0.5 0.5 Klebsiella pneumoniae (60) Ceftorazidie 0.25-4 2 16 Arteronam 20.0-0.5 20.05 20.05 20.05 Arteronam 20.0-0.5 20.05 20.05 20.05 Ceftoperazone 20.0-0.5 20.05 11 20.0-0.5 20.05 Ceftoperazone 20.00-0.5 20.05 1 20.00-0.5 20.05 20.05 Ceftoperazone 20.06-4 16 32.00 20.05		Apalcillin	4.0->128	8	16
Azreonam 50.06-2 32 200 0.3 Conferenzance 20.06-23 20.6 Celtazidine 20.06-0.5 20.125 0.125 Gentamicin 0.25-1 0.5 0.5 Klebsiella pneumoniae (60) Celtification 0.25-4 2 16 Apalellin 0.5-64 2 16 Apalellin 0.5-64 8 16 Proteinstructure 40.06-5 30.06 20.0 Celtazidine 20.06-0.5 30.06 20.0 Celtazidine 20.06-0.5 30.0 20.0 Celtazidine 20.06-0.1 20.0 20.0 Celtazidine 20.06-1 40.0 20.0 Celtazidine 20.06-1 40.0 20.0 Celtazidine 20.06-1 40.0 20.0 Celtazidine 20.06-1 40.0 20.0 20.0 Celtazidine 20.06-1 50.06 0.0.125 Celtazidine 20.06-1 50.06 0.0.25 Proteus mitabilis (70) Celtariante 20.06-0.125 20.0 8 8 8 Proteus mitabilis (70) Celtariante 20.06-0.125 20.0 6 20.06 Celtazidine 20.06-2.5 20.06 20.06 Celtazidine 20.06-0.125 20.0 20.0 Celtazidine 20.06-0.15 20.0 20.0 Celtazidine 20.06-1 20.0 Celtazidine 20.06-0.15 20.0 20.0 Celtazidine 20.06-0.15 20.0 Celtazidine 20.06-1 20.0 Celtazidine 20.06-0.15 20.0 Celtazidine 20.06-1 20.0 Celtazi		Piperacillin	1.0->128	8	32
Celaperatonne 90.12-5 12 06 4 125 Celaperatonne 50.06-0.5 2006 125 Gentanicin 0.25-1 0.5 0.5 Klebsiella preumoniae (60) Celipiranide 0.125-64 2 16 Apaciellin 0.5-64 8 16 Piperacillin 0.5-64 8 16 Piperacillin 0.5-64 8 16 Celipiranide 50.06-15 ±0.06 ±0.05 Celiparatone ±0.06-4 0.25 10 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.05 11 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.05 10 Celiparatone ±0.06-1 ±0.06 0.05 Proteus mirabilis (70) Celiparatone ±0.06-10 ±0.05 10 Celiparatone ±0.06-10 ±0.05 10 Celiparatone ±0.06-125 ±0.06 ±0.05 Celiparatone ±0.06-125 ±0.06 ±0.06 Celiparatone ±0.06-2 ±0.06 ±0.06 Celiparatone ±0.06-2 ±0.06 ±0.06 Celiparatone ±0.06-2 ±0.06 ±0.06 Celiparatone ±0.06-0.25 ±0.06 ±0.05 Celiparatone ±0.06-0.25 ±0.06 Celiparatone ±0.06-0.25 ±0.06 Celiparatone ±0.06-0.25 ±0.06 Celiparatone ±0.06-0.25 ±0.06 ±0.05 Celiparatone ±0		Aztreonam	$\leq 0.06 - 2$	≤0.06	0.5
$\begin{array}{c} Certualize = 00.6-0.5 & 10.132 & 0.123 \\ Certualize = 0.25-1 & 0.5 & 0.5 \\ Gentamicin = 0.25-1 & 0.5 & 0.5 \\ Gentamicin = 0.25-1 & 0.5 & 0.5 \\ Piperacilin = 0.25-44 & 2 & 16 \\ Apalcillin = 0.5-64 & 8 & 16 \\ Piperacilin = 0.06-8 & 0.25 & 1 \\ Celtraxone = 0.06-1 & 0.25 & 1 \\ Celtraxone = 0.5-1 & 0.06 & 0.1 & 125 \\ Celtraxone & 0.05-1 & 0.06 & 0.06 & 0.125 \\ Celtraxone & 0.06-1 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.125 & 0.06 & 0.06 & 0.125 & 0.06 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.06 & 0.125 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.25 & 0.06 & 0.05 & 0.06 & 0.25 & 0.06 & 0.05 & 0.06 & 0.25 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.05 & 0.06 & 0.125 & 0.06 & 0.125 & 0.06 & 0.05 & 0.06 & 0.25 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.05 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 & 0.06 & 0.05 & 0.06 & 0.06 $		Cetoperazone	0.123 - > 128	~0.06	4 0 125
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$ \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	Klebsiella pneumoniae (60)	Cefpiramide	0.125-64	2	16
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		Apalcillin	0.5-64	8	16
$ \begin{array}{c c} Aztreonam & \leq 0.06-0.5 & \leq 0.06 & < 0.05 \\ Ceftoprazone & \leq 0.06-0.5 & \leq 0.06 & 0.125 \\ Ceftriaxone & \leq 0.06-4 & 0.25 & 4 \\ 0.25 & 4 & 0.5 & 1 \\ \end{array} \\ \end{tabular} \begin{array}{c c} Morganella morgani (30) & Cefpiramide & 8.0-s128 & 16 & 32 \\ Aztreonam & 2.0-s128 & 12 & 32 \\ Aztreonam & \leq 0.06-1 & \leq 0.06 & 0.125 \\ Ceftoprazone & 0.5-32 & 1 & 4 \\ Aztreonam & \leq 0.06-1 & \leq 0.06 & 0.125 \\ Ceftoprazone & 0.5-32 & 1 & 4 \\ Ceftriaxone & \leq 0.06-1 & \leq 0.06 & 0.125 \\ Ceftoprazone & 0.25-1 & 0.25 & 0.5 \\ \end{array} \\ \end{tabular} \begin{array}{c c} Proteus mirabilis (70) & Cefpiramide & 1.0-128 & 8 & 8 \\ Aztreonam & \leq 0.06-1.25 & \leq 0.06 & \leq 0.06 \\ Ceftoprazone & 0.25-12 & 0.5 & 1 \\ Aztreonam & \leq 0.06-2.25 & \leq 0.06 & \leq 0.06 \\ Ceftoprazone & 0.25-3 & 1.06 & \leq 0.06 \\ Ceftoprazone & 0.25-3 & 1.06 & \leq 0.06 \\ Ceftoprazone & 0.25-48 & 1 & 2 \\ Ceftriaxone & \leq 0.06-2.2 & \leq 0.06 & \leq 0.06 \\ Ceftoprazone & 0.05-48 & 2 & 4 \\ Aztreonam & \leq 0.06-2.2 & \leq 0.06 & \leq 0.06 \\ Ceftoprazone & 0.5-8 & 2 & 4 \\ Aztreonam & \leq 0.06-2.5 & \leq 0.06 & \leq 0.06 \\ Ceftoprazone & 0.5-8 & 2 & 4 \\ Apalcillin & 1.0-128 & 8 & 32 \\ Apalcillin & 0.5-8 & 2 & 4 \\ Apalcillin & 0.5-8 & 2 & 4 \\ Aztreonam & \leq 0.06-2.5 & \leq 0.06 & 0.125 \\ Ceftrazone & 0.06-2.5 & \leq 0.06 & 0.125 \\ Ceftrazone & 0.06-2.5 & \leq 0.06 & 0.126 \\ Ceftoprazone & 0.5-8 & 2 & 4 \\ Apalcillin & 1.0-2128 & 4 & 128 \\ Apalcillin & 1.0-2128 & 1 & 2 \\ Providencia spp. (16) & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0-128 & 8 & 64 \\ Aztreonam & \leq 0.06-2 & 0.125 & 1 & 0.66 \\ Ceftrazone & 0.06-12 & 0.05 & 16 \\ Ceftrazone & 0.06-12 & 0.05 & 16 \\ \end{array}$		Piperacillin	1.064	4	32
Proteus vulgaris (20) Proteus vulgaris (20) Providencia spp. (16) Cefpiramide		Aztreonam	≤0.06-0.5	≤0.06	≤0.06
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		Cefoperazone	≤0.06-8	0.25	1
$ \begin{array}{c ccccc} Cetazolinic & $0.06-4 & 0.25 & 4 \\ \hline \begin{tabular}{ ccccc cccc } \hline Cetazolinic & $0.25-4 & $0.5 & 1 \\ \hline \end{tabular} & $0.25-8 & $0.5 & 1 \\ \hline \end{tabular} & $2.0-5-128 & 2 & 2 & 3 \\ \hline \end{tabular} & $2.0-5-128 & 2 & 2 & 1 & 4 & 2 & 2 & 1 & 4 & 2 & 2 & 1 & 4 & 2 & 2 & 1 & 4 & 2 & 2 & 1 & 4 & 2 & $2$$		Ceftriaxone	≤0.06-0.5	≤0.06	0.125
$ \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		Gentamicin	≤0.06–4 0.25–8	0.25 0.5	4
Apalcilin $2.0-5128$ 2 32 Piperacillin $0.5-64$ 1 8 Aztreonam $=0.06-1$ $=0.06$ $=50.06$ Ceftparaone $=0.06-1$ $=0.06$ 0.125 Ceftrazidime $=0.06-16$ $=0.06$ 0.5 Gentamicin $0.25-11$ 0.25 0.5 Proteus mirabilis (70) Ceftpiramide $1.0-128$ 8 8 Apalcillin $0.25-128$ 2 2 2 Apperacillin $0.25-128$ 0.5 1 2 Apperacillin $0.25-128$ 2 2 2 Apperacillin $0.25-128$ 0.6 $= 50.06$ $= 50.06$ Ceftriaxone $= 0.06-25$ $= 0.06$ $= 50.06$ $= 50.06$ Ceftriaxone $= 0.06-15$ $= 0.06$ $= 50.06$ $= 50.06$ Ceftriaxone $= 0.06-16$ 0.25 0.5 Proteus vulgaris (20) Ceftriaxone $= 50.06-15$ 0.25 0.5 Ceftriaxone $= 0.06-15$ 0.25 0.5 <t< td=""><td>Morganella morganii (30)</td><td>Cefpiramide</td><td>8.0–≤128</td><td>16</td><td>32</td></t<>	Morganella morganii (30)	Cefpiramide	8.0–≤128	16	32
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	5 5 ()	Apalcillin	2.0–≤128	2	32
Aztreonam =0.06-1 =0.06 =0.06 Ceforazone =0.06-16 =50.06 0.125 Cefrazidine =0.06-16 =50.06 0.5 Gentamicin 0.25-1 0.25 0.5 Proteus mirabilis (70) Cefpiramide 1.0-128 8 8 Apalcillin 0.25-128 2 2 Piperacillin 0.25-3128 0.5 1 Aztreonam =50.06-0.125 =50.06 =50.06 Cefpiranide =0.05-0.25 =50.06 =50.06 Cefpiranide =0.05-2 =50.06 =50.06 Cefpiranide =0.05-2 =50.06 =50.06 Cefpiranide =0.05-2 =50.06 =50.06 Cefpiranide =0.05-1 =0.25 0.5 Cefpiranide =0.06-15 =0.06 =0.06 Ceffirasone =0.06-125 =50.06 =0.125 Ceffirasone =0.06-125 =50.06 =0.128 Ceffirasone =0.06-25 =50.06 =0		Piperacillin	0.5-64	1	8
$ \begin{array}{c} Cefoperazone & 0.5-32 & 1 & 4 \\ Ceftriaxone & \pm 0.06-1 & \pm 0.06 & 0.125 \\ Ceftazidime & \pm 0.06-16 & \pm 0.06 & 0.5 \\ \hline Ceftazidime & \pm 0.06-16 & \pm 0.06 & 0.5 \\ \hline Ceftazidime & 0.25-1 & 0.25 & 0.5 \\ \hline Proteus mirabilis (70) & Cefpiramide & 1.0-128 & 8 & 8 \\ Apalcillin & 0.25-2128 & 0.5 & 1 \\ Apalcillin & 0.25-2128 & 0.5 & 1 \\ Aztreonam & \pm 0.06-0.125 & \pm 0.06 & \pm 0.06 \\ \hline Ceftazione & \pm 0.06-2.2 & \pm 0.06 & \pm 0.06 \\ \hline Ceftazione & \pm 0.06-2.2 & \pm 0.06 & \pm 0.06 \\ \hline Ceftazione & \pm 0.06-2.2 & 8 & 32 \\ \hline Proteus vulgaris (20) & Cefpiramide & 4.0-32 & 8 & 32 \\ Proteus vulgaris (20) & Cefpiramide & 4.0-32 & 8 & 32 \\ \hline Apalcillin & 1.0-8 & 4 & 4 \\ \hline Apalcillin & 1.0-8 & 2 & 4 \\ \hline Ceftriaxone & \pm 0.06-0.25 & \pm 0.06 & \pm 0.06 \\ \hline Cefoperazone & 0.5-8 & 2 & 4 \\ \hline Ceftriaxone & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & \pm 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & 0.06 & 0.125 \\ \hline Ceftrazidime & \pm 0.06-0.25 & 0.06 & 50.06 \\ \hline Ceftrazidime & \pm 0.06-0.25 & 0.05 & 16 \\ \hline Ceftrazidime & \pm 0.06-0.25 & 0.5 & 16 \\ \hline Ceftrazidime & \pm 0.06-0.25 & 0.5 & 16 \\ \hline Serratia marcescens (60) & Ceftrazidime & 0.025-32 & 0.5 & 16 \\ \hline Ceftrazidime & 0.025-32 & 0.5 & 8 \\ \hline Ceftrazidime & 0.025-32 & 0.5 & 8 \\ \hline Ceftrazidime & 0.025-32 & 0.5 & 8 \\ \hline Ceftrazidime & 0.025-32 & 0.5 & 8 \\ \hline Ceftrazidime & 0.06-0.25 & 0.06 & 0.125 \\ \hline Ceftrazidime & 0.06-0.25 & 0.06 $		Aztreonam	≤0.06–1	≤0.06	≤0.06
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Cefoperazone	0.5-32	1	4
Proteus mirabilis (70) Cefpiramide 1.0-128 8 8 8Apalcillin 0.25-1128 2 2 2Piperacillin 0.25-128 0.5 1Aztreonam $= 50.06-0.125 = 50.06$ $= 50.06Cefoperazone 0.25-8 1 2Ceftriaxone = 50.06-0.25 = 50.06 = 50.06Cefoperazone 0.25-8 1 2Proteus vulgaris (20)Cefpiramide 4.0-32 8 32Apalcillin 0.5-8 2 4 4Piperacillin 0.5-8 2 4 4Aztreonam = 50.06-0.25 = 50.06 = 50.06Cefoperazone 0.3-8 2 4 4Piperacillin 0.5-8 2 4 4Ceftriaxone = 50.06-0.25 = 50.06 = 50.06Cefoperazone 0.3-8 2 4 4Piperacillin 0.5-8 2 4 4Ceftriaxone = 50.06-0.25 = 50.06 = 10.25Ceftraixine = 50.06-0.25 = 50.06 = 10.25Ceftraixine = 50.06-1.25 = 10.60 = 1.25Ceftraixine = 50.06-1.25 = 10.60 = 1.25Ceftraixine = 50.06-1.25 = 1.28 = 1 = 128Apalcillin 1.0-5-128 = 1 = 5128Piperacillin 0.25-32 = 1.18Piperacillin 0.25-32 = 1.18 = 1 = 5128Azireonam = 50.06-0.125 = 50.06 = 50.06Cefoperazone 0.25-32 = 1.18 = 1.28Azireonam = 50.06-1.25 = 50.06 = 50.06Cefoperazone 0.25-32 = 1.18 = 1.28 = 1.28Apalcillin 1.0-5-128 = 1.28 = 1.28 = 1.28 = 1.28Apalcillin 1.0-5-128 = 1.28 = 1$		Ceftriaxone	≤0.06-1	≤0.06	0.125
$Proteus mirabilis (70) \qquad Cefpiramide 1.0-128 & 8 & 8 \\ Apalcillin 0.25->128 & 2 & 2 \\ Piperacillin 0.25->128 & 0.5 & 1 \\ Aztreonam 50.06-0.125 & 50.06 & 50.06 \\ Cefoperazone 0.25-8 & 1 & 2 \\ Ceffiranide \leq 0.06025 & \leq 0.06 & \leq 0.06 \\ Ceftazidine & \leq 0.06025 & \leq 0.06 & \leq 0.06 \\ Ceftazidine & \leq 0.06025 & \leq 0.06 & \leq 0.06 \\ Ceftazidine & 1.0-28 & 4 & 4 \\ Apalcillin & 1.0-8 & 4 & 4 \\ Piperacillin & 0.5-8 & 2 & 4 \\ Ceffiramide & 4.0-32 & 8 & 32 \\ Apalcillin & 0.5-8 & 2 & 4 \\ Ceffiramide & 0.06-1 & 0.25 & 0.06 & \leq 0.06 \\ Cefoperazone & 0.06-1 & 0.25 & 0.06 & = 0.06 \\ Cefoperazone & 0.06-1 & 0.25 & 0.06 & 0.125 \\ Ceffiramide & 4.0-128 & 4 & 128 \\ Aztreonam & < 0.06-1 & 0.25 & 0.06 & 0.125 \\ Gentamicin & 0.25-8 & 1 & 4 \\ Providencia spp. (16) & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0128 & 1 & 4 \\ Providencia spp. (16) & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0-2128 & 1 & 16 \\ Ceffiramide & 0.06-0.125 & < 0.06 & < 0.06 \\ Cefoperazone & 0.25-2 & 1 & 16 \\ Ceffiramide & 50.06-0.125 & < 0.06 & < 0.06 \\ Cefoperazone & 0.025-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \\ Serratia marcescens (60) & Cefpiramide & 8.0-2128 & 64 & >128 \\ Apalcillin & 1.0-2128 & 8 & 64 \\ Aztreonam & < 0.06-2128 & 0.25 & 2 \\ Ceffiraxione & < 0.06-2128 & 0.25 & 2 \\ Ceffiramide & 0.025-128 & 0.5 & 16 \\ Serratia marcescens (60) & Cefpiramide & 4.0-218 & 4 & 32 \\ Ceffiraxione & < 0.06-2128 & 0.25 & 2 \\ Gentamicin & 0.25-2128 & 0.5 & 2 \\ Cefforerazone & 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 0.5 & 2 \\ Cefforerazone & < 0.025-2128 & 2 & 8 \\ Piperacillin & 2.0-2128 & 2 & 8 \\ Pipe$		Ceftazidime	≤0.06–16	≤0.06	0.5
Proteus mirabilis (70) Cefpiramide $1.0-128$ 8 8 8 8 8 8 8 8 8 2 2 2 Piperacillin $0.25 > 128$ 0.5 1 $Aztreonam$ $= 0.06 - 0.125$ $= 0.06$ </td <td></td> <td>Gentamicin</td> <td>0.25-1</td> <td>0.25</td> <td>0.5</td>		Gentamicin	0.25-1	0.25	0.5
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Proteus mirabilis (70)	Cefpiramide	1.0-128	8	8
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Apalcillin	0.25->128	2	2
$ \begin{array}{c ccccc} Aztreonam & \leq 0.06-0.125 & \leq 0.06 & \leq 0.06 \\ Ceftoperazone & 0.25-8 & 1 & 2 \\ Ceftriaxone & \leq 0.06-0.25 & \leq 0.06 & \leq 0.06 \\ Ceftazidime & \leq 0.06-22 & \leq 0.06 & \leq 0.06 \\ Gentamicin & 0.125-8 & 1 & 2 \\ \end{array} \\ \hline Proteus vulgaris (20) & Cefpiramide & 4.0-32 & 8 & 32 \\ Apalcillin & 1.0-8 & 4 & 4 \\ Piperacillin & 0.5-8 & 2 & 4 \\ Aztreonam & \leq 0.06 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.5-8 & 2 & 4 \\ Ceftriaxone & \leq 0.06-1 & 0.25 & 0.5 \\ Ceftazidime & \leq 0.06-0.25 & \leq 0.06 & 0.125 \\ Gentamicin & 0.25-8 & 1 & 4 \\ \end{array} \\ \hline Providencia spp. (16) & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0->128 & 2 & >128 \\ Piperacillin & 0.5->128 & 1 & >128 \\ Piperacillin & 0.5->128 & 1 & >128 \\ Piperacillin & 0.125-32 & 0.5 & 16 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Cefoprazone & 0.06-25 & = 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Cefoperazone & 0.06-25 & = 0.06 & \leq 0.06 \\ Ceftazidime & \leq 0.06-25 & = 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Cefoperazone & 0.125-32 & 0.5 & 16 \\ Serratia marcescens (60) & Cefpiramide & 8.0->128 & 64 & >128 \\ Apalcillin & 1.0->128 & 32 & 128 \\ Piperacillin & 1.0->128 & 4 & 32 \\ Ceftraxone & \leq 0.06->128 & 0.25 & 1 \\ Cefoperazone & 1.0->128 & 4 & 32 \\ Ceftraxone & \leq 0.06->128 & 0.25 & 1 \\ Cefoperazone & 1.0->128 & 4 & 32 \\ Ceftraxone & \leq 0.06->128 & 0.5 & 8 \\ Ceftrazidime & 0.125->128 & 0.5 & 8 \\ Ceftrazidime & 0.05-128 & 0.5 & 8 \\ Ceftrazidime & 0.05-128 & 0.5 & 8 \\ Ceftrazidine & 0.06->128 & 0.5 & 8 \\ Ceftrazidine & 0.06->128 & 0.5 & 8 \\ Ceftrazidine & 0.06->128 & 0.5 & 8 \\ Ceftrazidine & 0.05-128 & 0.25 & 2 \\ Salmonella enteritidis (10) & Cefpiramide & 4.0->128 & 4 & 8 \\ Apalcillin & 2.0->128 & 2 & 8 \\ Piperacillin & 2.0->128 & 2 & 8 \\ Pipera$		Piperacillin	0.25->128	0.5	1
$Proteus vulgaris (20) \qquad \begin{array}{c} Cetoperazone \\ Cettriaxone \\ Cettriaxone \\ e 0.06-0.25 \\ conditione \\ e 0.06-2 \\ e 0.06 \\ conditione \\ e 0.06-2 \\ e 0.06 \\ e 0.06 \\ e 0.06 \\ c 0.06 \\ e $		Aztreonam	≤0.06-0.125	≤0.06	≤0.06
$ \begin{array}{c cccc} CeftraixOne & \leq 0.062.5 & \leq 0.060 & \leq 0.060 \\ CeftraixOne & \leq 0.062.5 & \leq 0.060 & \leq 0.060 \\ Gentamicin & 0.125-8 & 1 & 2 \\ \end{array} \\ \hline Proteus vulgaris (20) & Cefpiramide & 4.0-32 & 8 & 32 \\ Apalcillin & 1.0-8 & 4 & 4 \\ Piperacillin & 0.5-8 & 2 & 4 \\ Aztreonam & \leq 0.06 & \leq 0.060 & \leq 0.06 \\ Cefoperazone & 0.5-8 & 2 & 4 \\ Ceftriaxone & \leq 0.06-1 & 0.25 & 0.06 & 0.125 \\ Gentamicin & 0.25-8 & 1 & 4 \\ \hline Providencia spp. (16) & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0->128 & 2 & >128 \\ Piperacillin & 0.5-128 & 1 & >128 \\ Aztreonam & \leq 0.06 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceforiaxone & \leq 0.0625 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & \leq 0.06-2128 & 0.5 & 16 \\ Serratia marcescens (60) & Cefpiramide & 8.0->128 & 64 & >128 \\ Apalcillin & 1.0->128 & 8 & 64 \\ Aztreonam & \leq 0.06-2128 & 0.25 & 1 \\ Cefoperazone & 1.0->128 & 4 & 32 \\ Ceftriaxone & \leq 0.06->128 & 0.25 & 1 \\ Cefoperazone & 1.0->128 & 4 & 32 \\ Ceftriaxone & \leq 0.06->128 & 0.25 & 1 \\ Cefoperazone & 1.0->128 & 4 & 32 \\ Ceftriaxone & \leq 0.06->128 & 0.25 & 2 \\ Gentamicin & 0.5-64 & 1 & 32 \\ Salmonella enteritidis (10) & Cefpiramide & 4.0->128 & 4 & 8 \\ Apalcillin & 2.0->128 & 2 & 8 \\ Piperacillin & 2$		Cefoperazone	0.25-8	1	2
$ \begin{array}{c ccccc} Certazidine & $0.06-2 & $1.06 & $50.06 \\ Cettazidine & $0.125-8 & 1 & 2 \\ \hline \\ Proteus vulgaris (20) & Cefpiramide & $4.0-32 & $8 & $32 \\ Apalcillin & $1.0-8 & $4 & 4 & 4 \\ Piperacillin & $0.5-8 & $2 & 4 & 4 & 4 & 4 \\ Piperacillin & $0.5-8 & $2 & 4 & 2 & 4 & 2 & 4 & 2 & 6 $		Cetteridime	≤0.06-0.25	≤0.06	≤0.06 <0.06
$\begin{array}{c cccccc} Proteus vulgaris (20) & Cefpiramide & 4.0-32 & 8 & 32 \\ Apalcillin & 1.0-8 & 4 & 4 \\ Piperacillin & 0.5-8 & 2 & 4 \\ Aztreonam & \leq 0.06 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.5-8 & 2 & 4 \\ Ceftriaxone & \leq 0.06-1 & 0.25 & 0.5 \\ Ceftriaxione & \leq 0.06-1 & 0.25 & \leq 0.5 \\ Ceftriamide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0->128 & 2 & >128 \\ Piperacillin & 0.5->128 & 1 & >128 \\ Aztreonam & \leq 0.06 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & \leq 0.06-0.125 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & \leq 0.06-0.125 & \leq 0.06 & \leq 0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & \leq 0.06-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \\ \end{array}$		Gentamicin	0.125-8	≤0.06 1	≤0.08 2
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Proteus vulgaris (20)	Cefpiramide	4.0-32	8	32
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Apalcillin	1.0-8	4	4
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Piperacillin	0.5-8	2	4
$Serratia marcescens (60) \qquad \begin{array}{cccc} Cefopirazione & 0.5-8 & 2 & 4 \\ Ceftriaxone & \leq 0.06-1 & 0.25 & 0.5 \\ Ceftazidime & \leq 0.06-0.25 & \leq 0.06 & 0.125 \\ Gentamicin & 0.25-8 & 1 & 4 \\ \end{array}$		Aztreonam	≤0.06	≤0.06	≤0.06
$Serratia marcescens (60) Salmonella enteritidis (10) Ceftpiramide 4.0-128 4.05-0.25 \leq 0.06 0.125Gentamicin 0.25-8 1.44Providencia spp. (16)Ceftpiramide 4.0-128 4.128Apalcillin 1.0->128 2.2128Piperacillin 0.5->128 1.2128Aztreonam \leq 0.06 \leq 0.06 \leq 0.06 \leq 0.06Ceftoperazone 0.25-32 1.16Ceftriaxone \leq 0.06-0.125 \leq 0.06 \leq 0.06Ceftoperazone 0.125-32 0.516Ceftiraxine \leq 0.06-2 0.125 1.6Ceftiraxine \leq 0.06-2 0.125 1.6Ceftiraxine \leq 0.06-2 0.125 1.6Ceftiraxine \leq 0.06-2 0.125 1.6Ceftiraxine \leq 0.06-2 0.125 1.6Serratia marcescens (60) Ceftiramide 8.0->128 64 >128Apalcillin 1.0->128 32 1.28Piperacillin 1.0->128 4.0.25 1.1Ceftiraxone \leq 0.06->128 0.25 1.1Ceftiraxone \leq 0.06->128 0.25 1.1Ceftiraxone \leq 0.06->128 0.25 1.28Ceftiraxine \leq 0.06->128 0.25 2.2Gentamicin 0.5-64 1.32Salmonella enteritidis (10) Ceftiramide 4.0->128 4.8Apalcillin 2.0->128 2.8Piperacillin 2.0->128 2.8Piperacillin 2.0->128 2.8Piperacillin 2.0->128 2.8Piperacillin 2.0->128 4.8Aztreonam \leq 0.06-0.25 \leq 0.06 0.125Ceftoperazone 0.5-32 0.5 2.2$		Cefoperazone	0.5-8	2	4
$Serratia marcescens (60) \qquad Cefpiramide \leq 0.06-0.23 \leq 0.06 0.125Gentamicin 0.25-8 1 4Providencia spp. (16) Cefpiramide 4.0-128 4 128Apalcillin 1.0->128 2 >128Piperacillin 0.5->128 1 >128Aztronam \leq 0.06 \leq 0.06 \leq 0.06 \leq 0.06Cefoperazone 0.25-32 1 16Ceftriaxone \leq 0.06-0.125 \leq 0.06 \leq 0.06Ceftraidime \leq 0.06-2 0.125 1Gentamicin 0.125-32 0.5 16Serratia marcescens (60) Cefpiramide 8.0->128 64 >128Apalcillin 1.0->128 32 128Piperacillin 1.0->128 32 128Piperacillin 1.0->128 32 128Piperacillin 1.0->128 4 32Ceftriaxone \leq 0.06->128 0.25 1Cefoperazone 1.0->128 4 32Ceftriaxine 0.125-128 0.5 8Ceftraidime 0.125-128 0.5 2Gentamicin 0.5-64 1 32Salmonella enteritidis (10) Cefpiramide 4.0->128 4 8Aztreonam \leq 0.0628 2 8Piperacillin 2.0->128 2 8Apalcillin 2.0->128 2 8Ceftraidime 0.125-128 2 8Ceftraidime 0.125-128 2 8Aztreonam \leq 0.0628 2 8Piperacillin 2.0->128 2 0.06Piperacillin 2.0->128 2 8Piperacillin 2.0->128 2 0.06Piperacillin 2.0->128 2 0.06Piperacillin$		Ceftriaxone	≤0.06-1	0.25	0.5
$\begin{array}{c cccccc} Providencia {\rm spp. (16)} & Cefpiramide & 4.0-128 & 4 & 128 \\ Apalcillin & 1.0->128 & 2 &>128 \\ Piperacillin & 0.5->128 & 1 &>128 \\ Aztreonam & <0.06 & <0.06 & <0.06 \\ Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & <0.06-0.125 & <0.06 & <0.06 \\ Ceftazidime & <0.06-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \\ \end{array}$		Gentamicin	≤0.06–0.25 0.25–8	≤0.06 1	0.125 4
Apalcillin $1.0->128$ 2>128Piperacillin $0.5->128$ 1>128Aztreonam ≤ 0.06 ≤ 0.06 ≤ 0.06 Cefoperazone $0.25-32$ 116Ceftriaxone $\leq 0.06-0.125$ ≤ 0.06 ≤ 0.06 Ceftriaxone $\leq 0.06-2$ 0.125 1Gentamicin $0.125-32$ 0.5 16Serratia marcescens (60)Cefpiramide $8.0->128$ 64Apalcillin $1.0->128$ 32128Piperacillin $1.0->128$ 864Aztreonam $\leq 0.06->128$ 0.25 1Cefoperazone $1.0->128$ 864Aztreonam $\leq 0.06->128$ 0.25 1Cefoperazone $1.0->128$ 432Ceftraidime $0.125->128$ 0.25 2Gentamicin $0.5-64$ 132Salmonella enteritidis (10)Cefpiramide $4.0->128$ 48Apalcillin $2.0->128$ 28Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.2->128$ 28Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2	Providencia spp. (16)	Cefpiramide	4.0-128	4	128
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Apalcillin	1.0->128	2	>128
Aztreonam ≤ 0.06 ≤ 0.06 ≤ 0.06 Cefoperazone $0.25-32$ 116Ceftriaxone $\leq 0.06-0.125$ ≤ 0.06 ≤ 0.06 Ceftazidime $\leq 0.06-2$ 0.125 1Gentamicin $0.125-32$ 0.5 16Serratia marcescens (60)Cefpiramide $8.0->128$ 64Apalcillin $1.0->128$ 32128Piperacillin $1.0->128$ 864Aztreonam $\leq 0.06->128$ 0.25 1Cefoperazone $1.0->128$ 432Ceftriaxone $\leq 0.06->128$ 0.5 8Ceftriaxone $\leq 0.06->128$ 0.25 2Gentamicin $0.125->128$ 0.25 2Gentamicin $0.5-64$ 132Salmonella enteritidis (10)Cefpiramide $4.0->128$ 48Apalcillin $2.0->128$ 28Piperacillin $2.0->128$ 28Piperacillin $2.0->128$ 28Piperacillin $2.0->128$ 28Piperacillin $2.0->128$ 28Piperacillin $2.0->128$ 28Piperacillin $2.0->128$ 28Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2		Piperacillin	0.5->128	1	>128
$Serratia marcescens (60) \begin{pmatrix} Cefoperazone & 0.25-32 & 1 & 16 \\ Ceftriaxone & \leq 0.06-0.125 & \leq 0.06 & \leq 0.06 \\ Ceftazidime & \leq 0.06-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \\ \end{pmatrix}$		Aztreonam	≤0.06	≤0.06	≤0.06
$Serratia marcescens (60) \qquad \begin{array}{cccc} Ceftriaxone & \leq 0.06-0.125 & \leq 0.06 & \leq 0.06 \\ Ceftazidime & \leq 0.06-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \end{array}$		Cefoperazone	0.25-32	1	16
$Serratia marcescens (60) \qquad \begin{array}{cccc} Ceftazidime & \leq 0.06-2 & 0.125 & 1 \\ Gentamicin & 0.125-32 & 0.5 & 16 \end{array}$		Ceftriaxone	≤0.06-0.125	≤0.06	≤0.06
Serratia marcescens (60) Cefpiramide Apalcillin $8.0->128$ 64 >128 Apalcillin $1.0->128$ 32 128 Piperacillin $1.0->128$ 8 64 Aztreonam $\leq 0.06->128$ 0.25 1 Cefoperazone $1.0->128$ 4 32 Ceftriaxone $\leq 0.06->128$ 0.5 8 Ceftriaxone $\leq 0.06->128$ 0.5 8 Ceftriaxine $0.125->128$ 0.25 2 Gentamicin $0.5-64$ 1 32 Salmonella enteritidis (10) Cefpiramide $4.0->128$ 4 8 Piperacillin $2.0->128$ 2 8 Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2		Gentamicin	≤0.06-2 0.125-32	0.125 0.5	1 16
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Serratia marcescens (60)	Cefniramide	8 0_>128	64	>178
Piperacillin $1.0->128$ 8 64 Aztreonam $\leq 0.06->128$ 0.25 1 Cefoperazone $1.0->128$ 4 32 Ceftriaxone $\leq 0.06->128$ 0.5 8 Ceftazidime $0.125->128$ 0.25 2 Gentamicin $0.5-64$ 1 32 Salmonella enteritidis (10)Cefpiramide $4.0->128$ 4 8 Apalcillin $2.0->128$ 2 8 Piperacillin $2.0->128$ 2 8 Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2		Apalcillin	1.0 > 120	32	120
Aztreonam $\leq 0.06 -> 128$ 0.25 1Cefoperazone $1.0 -> 128$ 4 32 Ceftriaxone $\leq 0.06 -> 128$ 0.5 8Ceftazidime $0.125 -> 128$ 0.25 2Gentamicin $0.5 -64$ 1 32 Salmonella enteritidis (10)Cefpiramide $4.0 -> 128$ 48Apalcillin $2.0 -> 128$ 28Piperacillin $2.0 -> 128$ 28Aztreonam $\leq 0.06 - 0.25$ ≤ 0.06 0.125 Cefoperazone $0.5 - 32$ 0.5 2		Piperacillin	1.0->128	8	64
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Aztreonam	≤0.06–>128	0.25	1
$ \begin{array}{c cccc} Ceftriaxone & \leq 0.06->128 & 0.5 & 8 \\ Ceftazidime & 0.125->128 & 0.25 & 2 \\ Gentamicin & 0.5-64 & 1 & 32 \\ \end{array} \\ Salmonella enteritidis (10) & Cefpiramide & 4.0->128 & 4 & 8 \\ Apalcillin & 2.0->128 & 2 & 8 \\ Piperacillin & 2.0->128 & 2 & 8 \\ Piperacillin & 2.0->128 & 2 & 8 \\ Aztreonam & \leq 0.06-0.25 & \leq 0.06 & 0.125 \\ Cefoperazone & 0.5-32 & 0.5 & 2 \\ \end{array} $		Cefoperazone	1.0->128	4	32
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		Ceftriaxone	≤0.06->128	0.5	8
Gentamicin $0.5-64$ 1 32 Salmonella enteritidis (10) Cefpiramide Apalcillin $4.0->128$ 4 8 Piperacillin $2.0->128$ 2 8 Piperacillin $2.0->128$ 2 8 Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2		Ceftazidime	0.125->128	0.25	2
Salmonella enteritidis (10) Cefpiramide 4.0->128 4 8 Apalcillin 2.0->128 2 8 Piperacillin 2.0->128 2 8 Aztreonam ≤0.06-0.25 ≤0.06 0.125 Cefoperazone 0.5-32 0.5 2		Gentamicin	0.5–64	1	32
Aparentia $2.0-120$ 2 8Piperacillin $2.0->128$ 2 8 Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2	Salmonella enteritidis (10)		4.0->128	4	8
Aztreonam $2.0-7120$ 2 0 Aztreonam $\leq 0.06-0.25$ ≤ 0.06 0.125 Cefoperazone $0.5-32$ 0.5 2		Piperacillin	2.0->120 2.0->128	2	o Q
Cefoperazone 0.5–32 0.5 2		Aztreonam	≤0.06-0.25	≤ 0 .06	0.125
		Cefoperazone	0.5-32	0.5	2

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Organism (no. of isolates)	Antibiotic	MIC range	MIC ₅₀ (µg/ml)	MIC ₉₀ (ug/ml)
	Ceftriaxone	<0.06_0.25	<0.06	0 125
	Ceftazidime	0.25-1	0.5	0.125
	Gentamicin	0.25-1	0.5	1
Staphylococcus aureus (methicillin	Cefpiramide	2.0-4	2	4
susceptible) (30)	Apalcillin	2.0-128	8	64
	Piperacillin	1.0-128	16	128
	Aztreonam	>128	>128	>128
	Cefoperazone	2.0-8	4	8
	Ceftriaxone	2.0-4	4	4
	Ceftazidime	8.0-32	16	16
	Gentamicin	0.25–32	0.5	0.05
Staphylococcus aureus (methicillin	Cefpiramide	16-128	64	128
resistant) (20)	Apalcillin	64–>128	128	>128
	Piperacillin	128->128	>128	>128
	Aztreonam	>128	>128	>128
	Cetoperazone	32->128	128	>128
	Cettriaxone	32 -> 128	>128	>128
	Gentamicin	128 -> 128 0.25 - 128	>128 64	>128 64
			•	0
Staphylococcus epidermidis (30)	Cefpiramide	0.25-8	2	8
	Apalcillin	≤0.06-64	2	32
	Piperacillin	≤0.06-64 128 > 128	> 129	64 > 128
	Aztreonam	128->128	>128	>128
	Celtriaxone	0.5 >128	2	0 64
	Ceftazidime	0.3 = 2120 2.0-64	*	64
	Gentamicin	≤0.06–128	0.125	32
Streptococcus faecalis (30)	Cefniramide	8 0-32	16	32
Sirepiococcus faecuits (50)	Analcillin	2 0-8	4	4
	Piperacillin	2.0-8	4	4
	Aztreonam	>128	>128	>128
	Cefoperazone	16-64	32	64
	Ceftriaxone	128->128	>128	>128
	Ceftazidime	>128	>128	>128
	Gentamicin	8.0->128	16	32
Streptococcus pyogenes (10)	Cefpiramide	≤0.06-0.125	0.125	0.125
	Apalcillin	≤0.06-0.125	0.125	0.125
	Piperacillin	≤0.06-0.25	0.125	0.125
	Aztreonam	8.0–16	16	16
	Cefoperazone	0.125-0.25	0.125	0.25
	Ceftriaxone	≤0.06	≤0.06	≤0.06
	Gentamicin	≤0.06-0.25 1.0-8	0.125 4	0.125 8
Streptococcus agalactiae (10)	Cefpiramide	0.25-2	0.5	0.5
	Apalcillin	0.25-2	0.5	0.5
	Piperacillin	0.23-2	0.25	0.5 > 129
	Aztreonam	128->128	>128	>120
	Ceftriavane	<0.125-2	<0.25	<0.25
	Ceftazidime	0 5-2	0.5	0.5
	Gentamicin	16-64	16	32
Streptococcus preumoniae	Cefniramide	0 25-8	1	8
(nehicillin resistant) (9)	Apalcillin	0.125-8	2	8
(Perionini resistant) ())	Piperacillin	0.25–16	4	16
	Aztreonam	64->128	>128	>128
	Cefoperazone	0.5-8	2	8
	Ceftriaxone	0.125-4	1	4
	Ceftazidime	1.0-128	16	128
	Gentamicin	2.0-32	16	32

TABLE 1—Continued

Organism (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
Viridans group streptococci	Cefpiramide	0.25–2	0.5	2
(penicillin susceptible) (10)	Apalcillin	≤0.06–0.5	0.25	0.25
	Piperacillin	≤0.06–0.5	0.25	0.5
	Aztreonam	128->128	>128	>128
	Cefoperazone	0.125-1	0.5	1
	Ceftriaxone	≤0.06–0.5	0.125	0.5
	Ceftazidime	≤0.06–32	2	16
	Gentamicin	0.25-4	0.5	2
Viridans group streptococci	Cefpiramide	8.0-32	8	32
(penicillin resistant) (10)	Apalcillin	2.0-8	4	8
	Piperacillin	4.0-32	16	16
	Aztreonam	>128	>128	>128
	Cefoperazone	4.0–16	8	16
	Ceftriaxone	1.0-4	2	4
	Ceftazidime	16-64	16	32
	Gentamicin	2.0–16	8	16
Group G streptococci (10)	Cefpiramide	0.125-0.25	0.125	0.25
	Apalcillin	0.125	0.125	0.125
	Piperacillin	0.125	0.125	0.125
	Aztreonam	64	64	64
	Cefoperazone	0.25	0.25	0.25
	Ceftriaxone	≤0.06	≤0.06	≤0.06
	Ceftazidime	0.25	0.25	0.25
	Gentamicin	8.0	8	8
Listeria monocytogenes (20)	Cefpiramide	0.5-8	4	8
	Apalcillin	≤0.06–2	2	2
	Piperacillin	0.5–4	2	4
	Aztreonam	64–>128	>128	>128
	Cefoperazone	1.0-64	32	32
	Ceftriaxone	1.0->128	128	>128
	Ceftazidime	8.0->128	>128	>128
	Gentamicin	0.125-0.5	0.5	0.5

 TABLE 1—Continued

Princeton, N.J.; ceftriaxone, Hoffmann-La Roche Inc., Nutley, N.J.; cefoperazone, Pfizer Inc., Groton, Conn.; carbenicillin, Beecham Laboratories, Bristol, Tenn.; ceftazidime, Glaxo Laboratories, Fort Lauderdale, Fla.; cefsulodin, Abbott Laboratories, North Chicago, Ill.; and gentamicin, Schering Corp., Kenilworth, N.J. Antibiotic solutions were prepared daily as needed, and antibiotic-containing plates were inoculated within 18 h of preparation.

Susceptibility studies. MICs were determined by an agar dilution technique (16) with Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md.). The concentration of agar was increased to 4% with Bacto-Agar (Difco Laboratories, Detroit, Mich.) when testing Proteus sp. to prevent swarming. When streptococci were tested, Mueller-Hinton agar was supplemented with 5% sheep blood. Campylobacter jejuni was tested with brucella agar (BBL) supplemented with 10% sheep blood. For Haemophilus influenzae and N. gonorrhoeae, chocolate agar supplemented with 1% IsoVitaleX (BBL) was used. Overnight cultures of test organisms in Mueller-Hinton broth (BBL), Todd-Hewitt broth (for streptococci; BBL), or thioglycolate medium (for C. jejuni; GIBCO Diagnostics, Madison, Wis.) were diluted in fresh broth to approximately 107 CFU/ml. For H. influenzae and N. gonorrhoeae, fresh colonies from chocolate agar plates were dispersed in broth to the same density of organisms. For Streptococcus pneumoniae, fresh colonies from brucella agar plates were dispersed in broth to the same density. Inocula of approximately 10^4 CFU were applied with a

32-prong replicating device. Plates were examined for growth after 18 h of incubation at 37°C. A single colony or faint haze was ignored when determining endpoints. *C. jejuni* strains were incubated in a microaerophilic atmosphere (Campy

TABLE 2. Number of strains showing synergy, indifference, and antagonism for combinations of agents tested against gramnegative bacilli

Antibiotic	No. of strains showing synergy/indifference/ antagonism ^a			
combination	K. pneumoniae	E. cloacae	P. aeruginosa	
Cefpiramide and gentamicin	6/4/0	5/5/0	8/2/0	
Apalcillin and gentamicin	0/10/0	6/4/0	10/0/0	
Cefpiramide and cefoxitin	0/10/0	0/0/10	0/2/8	
Apalcillin and cefoxitin	0/10/0	0/2/8	0/1/9	
Piperacillin and cefoxitin	0/10/0	0/2/8	0/0/10	
Cefpiramide and piperacillin	0/10/0	0/10/0	1/9/0	
Apalcillin and piperacillin	0/10/0	3/7/0	2/8/0	

^a Numerals separated by shills represent the number of strains showing synergy, indifference, and antagonism, respectively.

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Excherichia coli resistant to gentamicin, tobranycin, and antikacin (15) Celpiramide (15) 0.5-128 1 2 128 Carbenicillin 2.0-226 3 2 23 2 Moxalactam 3.00-128 4 128 2 32 32 Moxalactam 3.00-218 0.25 32 32 32 32 Moxalactam 3.00-218 0.25 32 3	Bacteria (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
tobramycin, and amikacin (15) Apadcillin Carbencicilin (10) 0.5-128 (10) 2 128 (10)	Escherichia coli resistant to gentamicin,	Cefpiramide	0.5->128	4	32
Carbonic Carbonic Constraints Carbonic Carbonic Constraints Carbonic Carbonic Constraints Constaints Constraints <t< td=""><td>tobramycin, and amikacin (15)</td><td>Apalcillin</td><td>0.5->128</td><td>2</td><td>128</td></t<>	tobramycin, and amikacin (15)	Apalcillin	0.5->128	2	128
Prefacilini 10.12.13 4.35 1.23 Cefoperazione 50.06.218 0.125 0.5 Certinizone 50.06.2128 0.0125 0.5 Certinizone 50.06.2128 0.025 8 Certinizone 50.06.2128 0.05 1.12 4 Certinizone 50.06.2128 0.05 8 2.128 Certinizone 2.0.2128 8 >1.28 2.58 tobramycin, and amikacin (15) Ceftrianne 2.0.2128 1.8 >2.58 Movalactan 0.25.2128 1.8 >2.18 >1.28 Movalactan 0.25.2128 2 64 >1.28 Secratia marcescens resistant to first- and Ceftrianne 0.25.2128 2.6 64 2.56 Second-generation cephalosporins (10) Ceftriannite 3.0.212.8 4 32 64 2.56 Ceftrianne 0.25-64 1 8 2.2 1 2 Second-generation cephalosporins (10) Ceftriannite 8.0-128 <t< td=""><td></td><td>Carbenicillin</td><td>2.0->256</td><td>32</td><td>>256</td></t<>		Carbenicillin	2.0->256	32	>256
Catoperatione =:006-7:8 0.25 0.25 Maximum =:006-7:12 0.125 0.12 Ceftriaxone =:006-7:12 0.025 8 Pseudomonas aeruginosa resistant to gentamicin, tobramycin, and amikacin (15) Cefpiramide 2.0-2128 8 >128 Apalcillin 2.0-2128 12 4 128 225 Prereaillin 4.0-2128 16 >128 225 Prereaillin 4.0-2128 16 >128 226 Prereaillin 4.0-2128 16 >128 226 Mosalactan 0.2-2128 2 64 218 228 Secratia marcescens resistant to first- and second-generation cephalosporins (10) Cefpiramide 32-2128 64 >128 Ceforeazone 2.0-2128 1 16 25 2 Activitatione 0.25-46 0.5 2 1 2 Cefpiramide 30-2128 64 218 2 2 Actritaxitine 0.25-46 0.5		Piperacillin	1.0 - > 128	4 0.25	120
Azreonam =006->128 0125 2 Ceftrixtone =006->128 006 1 Ceftraidime =006->128 025 8 Pseudomonas aeraginosa resistant to gentamicin, tobranycin, and amikacin (15) Cefpiramide 2.0->128 8 >128 Carbenicillin 3.2->256 128 >256 128 >256 Carbenicillin 3.2->253 128 >128 >128 Carbenicillin 3.2->253 128 >128 >128 Ceforazone 4.0->128 16 >128 >128 Azreonam 4.0->128 16 >128 >128 Serratia marcezcene resistant to first- and second-generation cephalosporins (10) Cefipriamide 32->128 64 >128 Azreonam 0.12-8 0.25 2 64 256 Piperacillin 4.0->128 4 16 25 Second-generation cephalosporins (10) Cefipriamide 30->128 4 16 Ceforazone 0.12-8 0.25 2		Movalactam	≤0.00-32 <0.06-128	0.25	0.5
Ceftriaxone =0.06->128 =0.05 1 Cetazidine =0.05->128 0.25 8 Pseudomonas aeraginosa resistant to gentamicin, tobramycin, and amikacin (15) Cefpiramide 2.0->128 8 >128 Apalcillin 2.0->128 8 >128 >256 128 >225 Piperacillin 4.0->128 16 >128 >128 >128 Monalactan 0.0->128 12 >256 32 >128 Monalactan 0.0->128 12 >128 >128 >128 Monalactan 0.2->128 2 64 >128 >128 Second-generation cephalosporins (10) Cefpiramide 32->128 64 >128 Second-generation cephalosporins (10) Cefpiramide 16->128 4 15 Ceforazone 2.0->128 1 8 2 64 18 Actrixone 0.25-16 0.5 2 1 2 64 128 18 18 2 18 18		Åztreonam	≤0.06->128	0.125	2
$ \frac{1}{Certazidime} = \pm 0.06 -> 128 0.25 8 $ $ \frac{1}{28} = 0.25 8 + 128 -> 128 + 128$		Ceftriaxone	≤0.06->128	≤0.06	1
Pseudomonas aeruginosa resistant to gentamicin, tobramycin, and amikacin (15) Cerpiramide Parallillin Carbenicillin 32->236 2.0->128 8 >128 Corranycin, and amikacin (15) Cerpiramide Carbenicillin Cerperazine Autonom 4.0->128 16 >128 Serratia marcescens resistant to first- and second-generation cephalosporins (10) Cerpiramide Cerpiramide Cerparatine Autonom 32->128 64 >128 Serratia marcescens resistant to first- and second-generation cephalosporins (10) Cerpiramide Cerpiramide Cerpiramide Cerpiramide Cerpiramide Cerpiramide Autonom 32->128 64 >128 Serratia marcescens resistant to first- and second-generation cephalosporins (10) Cerpiramide Cerpira		Ceftazidime	≤0.06->128	0.25	8
tobramycin, and amikacin (15) Apalcillin Carbenicillin 2.0>128 4 128 Apalcillin 2.0>128 16 >128 Piperacillin 4.0>128 16 >128 Moxalactam 0.23>128 3 >128 Serratia marcescene resistant to first- and second-generation cephalosporins (10) Cerbinamide 32-128 2 64 Serratia marcescene resistant to first- and second-generation cephalosporins (10) Cerbinamide 32-128 64 >128 Serratia marcescene resistant to first- and second-generation cephalosporins (10) Cerbinamide 32-128 64 >128 Serratia marcescene resistant to ampicillin, carbenicillin, and cephalothin (8) Cerbinamide 32-326 1 1 Serratia marcescene resistant to ampicillin, carbenicillin, and cephalothin (8) Cerbinamide 80-128 1 2 Escherichia coli resistant to ampicillin, carbenicillin Cerbinamide 80-128 >128 >128 Cefinamoloe 40-32 8 8 16 128 Apalcillin 40-328 1 2 2	Pseudomonas aeruginosa resistant to gentamicin,	Cefpiramide	2.0->128	8	>128
Carbencialin 32-228 128 >128 Piperacilin 40->128 16 >128 Moxalactam 023->128 2 >128 Aztreonam 40->128 18 >128 Aztreonam 40->128 18 >128 Serratia marcescens resistant to first- and second generation cephalosporms (10) Cerbinaxine 023->128 64 >128 Second generation cephalosporms (10) Cerbinaxine 0.25-218 32 64 >128 Second generation cephalosporms (10) Cerbinamide 30->128 64 >128 Second generation cephalosporms (10) Cerbinamide 30->128 64 128 Second generation cephalosporms (10) Cerbinamide 80->128 4 32 Moxalactam 0.125-8 0.25 2 2 Cerbinamide 30->128 4 32 32 Moxalactam 0.125-8 0.25 2 1 16 Excherichia coli resistant to ampicillin, carbenicillin, and cephalothin (8) 728 64	tobramycin, and amikacin (15)	Apalcillin	2.0->128	4	128
Kebsiella pneumonia resistant to carbenicillin, arbenicillin, carbenicillin Cefpiramide 4.0-212 12 12 12 128 128 128 128 128 128 128		Carbenicillin	52->256	128	>230
		Piperacillin	4.0->128	16	>128
Accession Accession <t< td=""><td></td><td>Movalactam</td><td>4.0->128 0.25_>128</td><td>32</td><td>>120</td></t<>		Movalactam	4.0->128 0.25_>128	32	>120
Ceftriatione 2.0 > 128 128 > 128 Sernatia marcescens resistant to first- and second-generation cephalosporins (10) Cefpiamide 3.0 > 128 2 64 Second-generation cephalosporins (10) Cefpiamide 3.0 > 128 4 16 Composition (10) Cefpiamide 3.0 > 128 4 16 Composition (10) Cefpiamide 3.0 > 128 4 16 Composition (10) Cefpiamide 0.125-4 0.25 2 Cefpiamide 0.25-4 0.5 4 128 Autrenonam 0.125-8 0.25 1 2 Cefpiamide 0.5-2 1 2 1 1 and cephalothin (8) Cefpiamide 8.0-128 >128 >128 Piperacilin 16-32 8 16 128 32 and cephalothin (8) Cefpiamide 4.0-32 8 16 10.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25 <		Aztreonam	4.0->128	8	>128
		Ceftriaxone	2.0->128	128	>128
Serratia marcescens resistant to first- and second-generation cephalosporins (10) Cefpiramide Apalcillin (Carbenicillin extensional Carbenicillin (10) 32-2128 (10) 64 (21) >128 (21) Second-generation cephalosporins (10) Cefpiramide (10) 32-2128 (20) 64 (21) >128 (21) 32 (21) 64 (21) Second-generation cephalosporins (10) Cefpiramide (21) 32-2128 (21) 4 (21) 32 (21) 64 (21) Second-generation cephalosporins (10) Cefpiramide (21) 32-2128 (22) 4 (21) 32 (21) 64 (22) 22 (21) Second-generation cephalosporins (10) Cefpiramide (21) 0.25-4 (22) 0.25 (22) 1 (22) 1 (21) Escherichia coli resistant to ampicillin, carbenicillin and cephalothin (8) Cefpiramide (20) 8.0-128 (26) 64 (22) 128 (22) 2128 (26) Klebsiella pneumonia resistant to carbenicillin and cephalothin (9) Cefpiramide (20) 10.25-0 (25) 0.25 (25) 0.25 (25) 0.25 (25) Enterobacter cloacce resistant to carbenicillin and cephalothin (9) Cefpiramide (20) 10.25-8 (25) 0.25 (25) 128 (25) 128 (26) Enterobacter cloacce resistant to carbenicillin and cephalothin (9) C		Ceftazidime	0.25->128	2	64
second-generation cephalosporins (10) Apalcillin Carbenicillin Carbenicillin (10->128) 32 (25) 64 (25) 25 (25) Representing Carbenicillin (10->128) 4 16 (26) 18 (26) 4 16 (26) Bigeneration Carbenicillin (10->128) 0.25-128 (20) 4 32 (20) 4 32 (20) Escherichia coli resistant to ampicillin, carbenicillin and cephalothin (8) Cefpiramide (20) 8.0-128 (20) 64 128 (20) Escherichia coli resistant to ampicillin, carbenicillin and cephalothin (8) Cefpiramide (20) 8.0-128 (20) 64 128 (20) Piperacillin and cephalothin (8) Cefpiramide (20) 8.0-128 (20) 64 128 (21) 22 28 (22) 23 (22) 23 (22) 23 (22) 23 (22) 23 (22) 23 (22) 0.25 (20) 0.25 (22) 12 (22) <td>Serratia marcescens resistant to first- and</td> <td>Cefpiramide</td> <td>32->128</td> <td>64</td> <td>>128</td>	Serratia marcescens resistant to first- and	Cefpiramide	32->128	64	>128
Klebsiella pneumonia resistant to carbenicillin Cefpiramide 16.0->128 4 16 Cefoperazone 2.0->128 4 32 Moxalactam 0.125-8 0.25 4 32 Moxalactam 0.125-8 0.25 4 32 Ceftriarione 0.25-64 1 8 Aztreonam 0.125-8 0.25 2 1 16 Ceftrazidime 0.25-16 0.5 2 Ininpenem 0.5-2 1 16 Ceftrazidime 0.25-16 0.5 2 Ininpenem 0.5-2 1 16 Ceftrazidime 0.25-16 0.5 2 Ininpenem 0.5-2 1 16 Ceftrazidime 1.0-32 1 16 Ceftrazidime 1.0-32 1 16 Ceftrazidime 0.25-16 0.5 2 Ceftrazidime 0.25-2 1 16 Ceftrazidime 0.25-2 1 16 Ceftrazidime 0.25-2 1 Ceftrazidime 0.125-0 5 0.125 0.125 Ceftrazidime 0.125-0 5 0.125 0.125 Ceftrazidime 0.125-0 5 0.125 0.125 Ceftrazidime 0.125-8 0.25 0.25 Ceftrazidime 0.125-0 5 0.25 0.25 Ceftrazidime 0.125-8 0.25 0.25 Ceftrazidime 0.125-1 2 Ceftrazidime 0.125-1 2 Ceftrazidime 0.125-1 2 Ceftrazidime 0.125-1 2 Ceftrazidime 0.125-1 12 Ceftrazidime 0.125-2 2 Ceftrazidime 0.125-2 2 Ceftrazidime 0.125-2 2 Ceft	second-generation cephalosporins (10)	Apalcillin	8.0->128	32	64
Klebsiella pneumonia resistant to carbenicillin, and cephalothin (9) Futersolution		Carbenicillin	16->256	64	256
Cetoperazone 0.25-64 1 8 Aztreonam 0.125-8 0.25 2 Ceftrizione 0.25-64 0.5 4 Ceftrizione 0.25-16 0.5 2 Inipenen 0.5-2 1 2 Gentamicin 1.0-32 1 16 Escherichia coli resistant to ampicillin, carbenicillin, and cephalothin (8) Cefpiramide 8.0-128 64 128 Piperacillin 16-3128 >128 >128 >128 Ceforizance 4.0-32 8 32 Ceforitin 4.0-32 8 16 Octivin 4.0-32 8 16 0.06-4 0.125 0.125 0.25 Ceforizone 0.06-4 0.125 0.125 0.25<		Piperacillin	4.0->128	4	10
Moxauctum 0.125-8 0.25 2 Aztreonam 0.125-44 0.5 4 Ceftraxone 0.25-64 0.5 2 Imipenem 0.5-2 1 2 Gentamicin 1.0-32 1 16 Escherichia coli resistant to ampicillin, and cephalothin (8) Apticillin 16->128 >128 >128 Piperacillin 16->128 >128 >128 >128 >128 Cefoxitin 4.0-32 4 8 32 Cefoxitin 4.0-32 4 8 Cefoxitin 4.0-32 4 8 16 Moxalactam 0.125 0		Cetoperazone	2.0->128	4	32
Klebsiella pneumonia resistant to carbenicillinand cephalothin (9) $Klebsiella pneumonia resistant to carbenicillinand cephalothin (9)Klebsiella pneumonia resistant tocefiraxione = 50.06-0.5 0.25 0.25 0.25 0.25 0.25 0.25 0.25 0$		Moxalactam	0.23-04	0.25	2
Ceftariation 0.25-16 0.5 2 Imipenem 0.3-2 1 2 Gentamicin 10-32 1 1 and cephalothin (8) Piperacillin 16-3128 >128 >128 Apalcillin 16-3128 >128 >128 >128 Ceforamide 4.0-32 8 32 Ceforamide 4.0-32 8 32 Ceforation 4.0-32 8 32 Ceforation 4.0-32 8 32 Ceforation 4.0-32 8 32 Ceforation 0.125-0.5 0.125 0.25 Aztreonam =0.06-4 0.125-8 0.025 0.25 0.25 Imipenem 0.25-0.5 0.25 0.25 0.25 0.25 Imipenem 0.25-0.5 0.25<		Ceftriaxone	0.125-64	0.5	4
		Ceftazidime	0.25-16	0.5	2
		Imipenem	0.5-2	1	2
		Gentamicin	1.0-32	1	16
and cephalothin (8) $Apalcillin 16->128 >128 >128 >128 Piperacillin 16->128 >128 >128 >128 Cefamandole 4.0-32 8 32 Cefoxitin 4.0-32 4 8 16 Moxalactam 0.125-0.5 0.125 0.25 Aztreonam \leq 0.06-4 0.125 0.122 0.122Ceftraixone \leq 0.06-1 \leq 0.066 \leq 0.06 Ceftraixone \leq 0.06-1 \leq 0.066 \leq 0.06 = 0.06 Ceftraixone \leq 0.06-1 \leq 0.025 = 0.25$	Escherichia coli resistant to ampicillin, carbenicillin,	Cefpiramide	8.0-128	64	128
$Enterobacter cloacae resistant to carbenicillin Cerbanadole 16->128 >128 >128 >128 32 Cefanandole 4.0-32 8 32 Cefoxitin 4.0-32 4 8 16 Moxalactam 0.125-0.5 0.125 0.25 Aztreonam \leq 0.06-1 \leq 0.06 \leq 1.0.6Ceftraixone \leq 0.06-1 \leq 0.06 \leq 0.0.6Ceftraixone \leq 0.06-1 \leq 0.06 \leq 1.0.6Ceftraixone \leq 0.06-1 \leq 0.25 = 0.25Imipenem 0.25-0.5 = 0.25 = 0.25Ceftraixone \leq 0.06-1 \leq 0.06 \leq 1.0.6Ceftraixone \leq 0.06-1 \leq 0.25 = 0.25Ceftraixone \leq 0.06-1 \leq 0.25 = 0.25Ceforenamole 1.0-128 = 16 > 128Piperacillin 4.0->128 = 16 > 128Ceforamole 1.0-128 = 16 = 128Ceforation 0.25-32 = 4 = 32Ceforitin 4.0->128 = 16 = 128Ceforenamole 0.25-32 = 4 = 32Ceftraixone \leq 0.06-0.5 = 0.125 = 1Aztreonam \leq 0.06-0.5 = 0.125 = 1Aztreonam \leq 0.06-0.5 = 0.125 = 1Aztreonam \leq 0.06-0.5 = 0.125 = 0.25Ceftraixone \leq 0.06-0.5 = 0.125 = 0.25Ceftraixone \leq 0.06-0.5 = 0.125 = 1Aztreonam \leq 0.06-0.5 = 0.125 = 0.25Ceftraixone \leq 0.25-128 = 32 = 128Moxalactam 0.125-32 = 16 = 16Aztreonam 0.25-42 = 16 = 128Ceftraixone 0.25-128 = 32 = 128Ceftr$	and cephalothin (8)	Apalcillin	16->128	>128	>128
$Enterobacter cloacae resistant to carbenicillin and cefamandole (9) \begin{array}{ccccccccccccccccccccccccccccccccccc$		Piperacillin	16->128	>128	>128
		Cefamandole	4.0-32	8	52
$Enterobacter cloacae resistant to carbonic illin and cefamandole (9) Enterobacter cloacae resistant to carbonic illin and cefamandole (9) Enterobacter cloacae resistant to carbonic illin definition Cefpiramide = 16->128 = 128 \\ Cefpiramide = 0.125-48 \\ Cefpiramide = 16->128 \\ Cefpiramide = 16->128 \\ Cefpiramide = 10->128 \\ Cefpiramide = 10->128 \\ Ceforitin = 0.125-48 \\ Ceforerazone \\ Co->128 \\ $		Cefonerazone	4.0-32	*	16
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Moxalactam	0.125-0.5	0.125	0.25
		Aztreonam	≤0.06-4	0.125	0.125
$Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae resistant to Carbonicillin and cefamandole (9) \\ Enterobacter cloacae conduct and conduct and cefamandole (9) \\ Entero$		Ceftriaxone	≤0.06-1	≤0.06	≤0.06
		Ceftazidime	0.125-8	0.25	0.25
$Enterobacter cloacae resistant to carbonic (9) Gentamicin 0.25-2 1 22 Klebsiella pneumonia resistant to carbonicillin Cefpiramide 16.0->128 32 >128 Apalcillin 4.0->128 16 >128 Piperacillin 4.0->128 16 228 Cefamandole 1.0-128 16 64 Cefoyerazone 0.25-32 4 32 Moxalactam 0.125-8 0.125 1 Aztreonam \leq 0.06-0.5 0.125 0.25Ceftraixone \leq 0.06-0.5 0.125 0.25Ceftraidime 0.125-4 1 2Imipenem 0.125-1 0.25 0.5Ceftaradime 16->128 64 >128Piperacillin 4.0->128 64 >128Cefoyerazone 0.5-32 2 32Enterobacter cloacae resistant tocarbenicillin and cefamandole (9)Apalcillin 4.0->128 64 >128Moxalactam 0.125-32 16 16Apalcillin 4.0->128 64 >128Cefoperazone 2.0->128 32 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 128 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 16 16Aztreonam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.25-64 16 32Ceftraixone 0.25-128 32 128Moxalactam 0.125-32 0.5 1$		Imipenem	0.25-0.5	0.25	0.25
		Gentamicin	0.25–2	1	2
and cephalothin (9)Apacilin $4.0-2126$ 10 2128 Piperacillin $4.0-2128$ 32 >128 Cefamandole $1.0-128$ 16 128 Cefoxitin $4.0-2128$ 16 64 Cefoyerazone $0.25-32$ 4 32 Moxalactam $0.125-8$ 0.125 1 Aztreonam $\leq 0.06-0.5$ 0.125 0.25 Ceftriaxone $\leq 0.06-0.5$ 0.125 0.25 Ceftriaxone $\leq 0.06-0.5$ 0.125 0.25 Ceftriaxone $< 0.06-0.5$ 0.125 0.25 Ceftriaxone $< 0.06-0.5$ 0.125 0.25 Ceftazidime $0.125-4$ 1 2 Imipenem $0.125-1$ 0.25 0.5 Gentamicin $0.5-32$ 2 32 Enterobacter cloacae resistant to carbenicillin and cefamandole (9)Cefpiramide $16->128$ >128 Piperacillin $4.0->128$ 64 >128 Piperacillin $4.0->128$ 32 128 Moxalactam $0.125-32$ 16 16 Aztreonam $0.25-64$ 16 32 Ceftriaxone $0.25-128$ 32 128 Moxalactam $0.25-128$ 32 128 Ceftraidime $1.0-128$ 32 128 Imipenem $0.5-2$ 0.5 1	Klebsiella pneumonia resistant to carbenicillin	Cefpiramide	16.0->128	32	>128
Enterobacter cloacae resistant to carbenicillin and cefamandole (9) Enterobacter cloacae resistant to carbenicillin and cefamandole (9) Enterobactam 0.125-4 10.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25	and cephalothin (9)	Apalcillin	4.0->128	10	>128
Enterobacter cloacae resistant to certaining to certain the certain the certain to certain the certain to carbenicillin and cefamandole (9) $Enterobacter cloacae resistant to certain the certain to certain the certain to certain to certain to certain to certain to certain to certain the certain the certain to certain the certain to certain the certain t$		Cefamandole	1 0-128	16	128
$ \begin{array}{cccc} Cefoperazone & 0.25-32 & 4 & 32 \\ Moxalactam & 0.125-8 & 0.125 & 1 \\ Aztreonam & \leq 0.06-0.5 & 0.25 & 0.25 \\ Ceftriaxone & \leq 0.06-0.5 & 0.125 & 0.25 \\ Ceftraidime & 0.125-4 & 1 & 2 \\ Imipenem & 0.125-1 & 0.25 & 0.5 \\ Gentamicin & 0.5-32 & 2 & 32 \\ \end{array} $		Cefoxitin	4.0->128	16	64
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		Cefoperazone	0.25-32	4	32
$\begin{array}{c cccc} Aztreonam & \leq 0.06-0.5 & 0.25 & 0.25 \\ Ceftriaxone & \leq 0.06-0.5 & 0.125 & 0.25 \\ Ceftrazidime & 0.125-4 & 1 & 2 \\ Imipenem & 0.125-1 & 0.25 & 0.5 \\ Gentamicin & 0.5-32 & 2 & 32 \\ \end{array}$ $\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Moxalactam	0.125-8	0.125	1
$\begin{array}{c cccc} Ceftriaxone & \leq 0.06-0.5 & 0.125 & 0.25 \\ Ceftazidime & 0.125-4 & 1 & 2 \\ Imipenem & 0.125-1 & 0.25 & 0.5 \\ Gentamicin & 0.5-32 & 2 & 32 \\ \end{array}$ $\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Aztreonam	≤0.06-0.5	0.25	0.25
$\begin{array}{cccc} Ceftazidime & 0.125-4 & 1 & 2 \\ Imipenem & 0.125-1 & 0.25 & 0.5 \\ Gentamicin & 0.5-32 & 2 & 32 \end{array}$ $Enterobacter cloacae resistant to carbenicillin and cefamandole (9) \qquad Apalcillin & 4.0->128 & 64 & >128 \\ Piperacillin & 4.0->128 & 64 & >128 \\ Piperacillin & 4.0->128 & 64 & >128 \\ Cefoperazone & 2.0->128 & 32 & 128 \\ Moxalactam & 0.125-32 & 16 & 16 \\ Aztreonam & 0.25-64 & 16 & 32 \\ Ceftraixone & 0.25-128 & 32 & 128 \\ Ceftraixone & 0.25-128 & 32 & 128 \\ Ceftraixone & 0.25-128 & 32 & 128 \\ Ceftraizdime & 1.0-128 & 32 & 128 \\ Imipenem & 0.5-2 & 0.5 & 1 \end{array}$		Ceftriaxone	≤0.06-0.5	0.125	0.25
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Ceftazidime	0.125-4	1	2
$\begin{array}{c ccccc} Enterobacter cloacae resistant to carbenicillin and cefamandole (9) & Apalcillin & 4.0->128 & 64 &>128 \\ Piperacillin & 4.0->128 & 64 &>128 \\ Piperacillin & 4.0->128 & 64 &>128 \\ Cefoperazone & 2.0->128 & 32 & 128 \\ Moxalactam & 0.125-32 & 16 & 16 \\ Aztreonam & 0.25-64 & 16 & 32 \\ Ceftriaxone & 0.25-128 & 32 & 128 \\ Ceftaizdime & 1.0-128 & 32 & 128 \\ Imipenem & 0.5-2 & 0.5 & 1 \end{array}$		Gentamicin	0.125-1 0.5-32	2	32
$\begin{array}{c} \text{Carbenicillin and cefamandole (9)} \\ Carbenici$	Enterphantan diagona registert to	Cefniramide	16->128	>128	>128
Piperacillin 4.0->128 64 >128 Cefoperazone 2.0->128 32 128 Moxalactam 0.125-32 16 16 Aztreonam 0.25-64 16 32 Ceftriaxone 0.25-128 32 128 Ceftraidime 1.0-128 32 128 Imipenem 0.5-2 0.5 1	carbenicillin and cefamandole (9)	Apalcillin	4.0->128	64	>128
Cefoperazone2.0->12832128Moxalactam0.125-321616Aztreonam0.25-641632Ceftriaxone0.25-12832128Ceftazidime1.0-12832128Imipenem0.5-20.51		Piperacillin	4.0->128	64	>128
Moxalactam0.125-321616Aztreonam0.25-641632Ceftriaxone0.25-12832128Ceftazidime1.0-12832128Imipenem0.5-20.51		Cefoperazone	2.0->128	32	128
Aztreonam0.25-641632Ceftriaxone0.25-12832128Ceftazidime1.0-12832128Imipenem0.5-20.51		Moxalactam	0.125-32	16	16
Cettriaxone 0.25-128 32 128 Ceftazidime 1.0-128 32 128 Imipenem 0.5-2 0.5 1		Aztreonam	0.25-64	16	32
$\begin{array}{cccc} Certazidime & 1.0-128 & 52 & 120 \\ Imipenem & 0.5-2 & 0.5 & 1 \end{array}$		Ceftriaxone	0.25-128	32 32	128
		Lenazidime	1.0-120	05	120
Gentamicin 0.5–1 0.5 1		Gentamicin	0.5-1	0.5	i

TABLE 3. Comparative in vitro activities of antibiotics against resistant organisms

Bacteria (no. of isolates)	Antibiotic	MIC range (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
Pseudomonas aeruginosa resistant to	Cefpiramide	4.0->128	16	64
carbenicillin (8)	Apalcillin	4.0->128	16	64
	Piperacillin	16.0->128	32	128
	Cefoperazone	16.0->128	32	128
	Moxalactam	8.0->128	64	128
	Aztreonam	8.0->128	16	>128
	Ceftriaxone	8.0->128	64	>128
	Ceftazidime	2.0->128	4	16
	Imipenem	4.0->128	4	>128
	Gentamicin	4.0->128	4	128

 TABLE 3—Continued

Pak II; BBL), and N. gonorrhoeae strains were incubated in 5% CO₂. All other strains were incubated in room air.

Antibiotic combinations were tested in a checkerboard agar dilution matrix. Synergism was said to be present when the MIC of each drug tested in combination was fourfold or more lower than the MIC of each drug tested individually. Antagonism of drug A by drug B was said to be present when the MIC of drug A was fourfold or more higher in the presence of B than in its absence. Indifference was said to be present when the criteria for neither synergism nor antagonism were met.

RESULTS

Susceptibility studies. Results of agar dilution susceptibility studies are shown in Table 1. Except for ceftazidime, cefpiramide was the most active cephalosporin tested against P. aeruginosa. Against other nonfermenters, its activity was generally comparable to that of cefoperazone. However, against most members of the Enterobacteriaceae, cefpiramide was less active than the other cephalosporins tested. Against gram-positive organisms, the pattern of activity of cefpiramide was very similar to that of cefoperazone, and against Listeria monocytogenes it was the most active cephalosporin tested (MIC for 90% of the strains tested $[MIC_{90}] = 8 \ \mu g/ml$). C. jejuni strains were resistant to cefpiramide, with MICs of $\geq 128 \ \mu g/ml$ for all of the 24 strains tested. When cefpiramide was tested against three strains of Yersinia enterocolitica, the MICs obtained ranged from 8.0 to 32.0 μ g/ml, higher than those obtained for any other antibiotic in this study.

Apalcillin was the most active penicillin tested against *P. aeruginosa*, with activity equal to that of ceftazidime against these isolates (MIC₉₀ = 8 μ g/ml). Against other nonfermen-

ters, the activity of apalcillin either equaled or exceeded those of both piperacillin and mezlocillin (data for mezlocillin not shown). Strains of H. influenzae that produced β-lactamase were resistant to all three penicillins; against β-lactamase-negative strains, apalcillin was slightly less active than either piperacillin or mezlocillin. The activity of apalcillin against members of the Enterobacteriaceae was comparable to those of the other penicillins. Although it was the most active of the three penicillins tested against L. monocytogenes (MIC₉₀ = 2.0 μ g/ml), against other grampositive organisms, apalcillin was comparable to piperacillin and only slightly less active than mezlocillin (data not shown). Apalcillin exhibited poor activity against 24 strains of C. jejuni, with an MIC₅₀ of 32 µg/ml and an MIC₉₀ of 128 µg/ml (MIC range, 1.0 to 128.0 µg/ml). Against three strains of Y. enterocolitica, the range of MICs obtained for apalcillin was 8 to 16 µg/ml, higher than those obtained for any other antibiotic in this study with the exception of cefpiramide.

Antibiotic combinations. The results of testing these antibiotics in combination with other agents are presented in Table 2. The combination of cefpiramide and gentamicin synergistically inhibited 80% of *P. aeruginosa* strains, 50%of *Enterobacter cloacae* strains, and 60% of *Klebsiella pneumoniae* strains tested. Similarly, the combination of apalcillin and gentamicin synergistically inhibited 100% of *P. aeruginosa* and 60% of *E. cloacae* strains tested but none of the *K. pneumoniae* strains tested. However, cefoxitin antagonized the activity of cefpiramide against 100% of *E. cloacae* and 80% of *P. aeruginosa* strains. Similarly, cefoxitin antagonized the activity of apalcillin against 80% of *E. cloacae* and 90% of *P. aeruginosa* strains tested. Neither cefpiramide nor apalcillin antagonized the activity of any other

B-Lactamase	MIC (µg/ml) of:					
type	Cefpiramide	Apalcillin	Piperacillin	Cefoperazone	Ceftazidime	Imipenem
None	4	2	16	16	2	4
TEM-1	64	>128	>128	128	4	4
TEM-2	128	>128	>128	128	2	4
OXA-1	32	128	>128	16	2	4
OXA-2	64	>128	>128	64	8	4
OXA-3	>128	>128	>128	>128	16	4
PSE-1	32	128	>128	64	2	4
PSE-2	128	128	>128	>128	2	4
PSE-3	8	64	128	32	2	4
PSE-4	32	>128	>128	128	2	4

TABLE 4. Antimicrobial susceptibility of plasmid-containing strains of P. aeruginosa PU21

drug with which it was combined against any of these strains (Table 2).

Activity against resistant isolates. The results of susceptibility testing against selected strains of gram-negative bacilli resistant to multiple antibiotics are presented in Table 3. When tested against members of the *Enterobacteriaceae* resistant to other β -lactam agents, apalcillin and cefpiramide were significantly less active than moxalactam, ceftazidime, ceftriaxone, aztreonam, and imipenem. However, against carbenicillin-resistant strains of *P. aeruginosa*, both apalcillin and cefpiramide were slightly more active than the other agents tested, with the exception of ceftazidime.

In otherwise isogenic strains of *P. aeruginosa*, the presence of any one of nine plasmid-mediated β -lactamases adversely affected the activities of both cefpiramide and apalcillin (Table 4).

DISCUSSION

This study demonstrated the marked activity of both cefpiramide and apalcillin against *P. aeruginosa*. The activities of these two agents in this regard are comparable to those of the most active of the currently available β -lactams. Against a broad range of other gram-negative and gram-positive organisms, the activities of cefpiramide and apalcillin were sufficient to be clinically useful. However, against members of the *Enterobacteriaceae*, cefpiramide was the least active cephalosporin tested. The in vitro susceptibility results obtained in this study for both agents are in general agreement with those obtained by other investigators (5, 6, 8, 12–14).

Against strains selected for multiple resistance, neither cefpiramide nor apalcillin appeared to offer a significant advantage over other currently available agents. Similarly, when tested against a series of otherwise isogenic strains of *P. aeruginosa*, the activities of both cefpiramide and apalcillin were markedly reduced in the presence of each of nine different plasmid-mediated β -lactamases, although the activity of cefpiramide was less affected than that of apalcillin. This is consistent with previous work demonstrating susceptibility of both apalcillin and cefpiramide to hydrolysis by a number of β -lactamases (8, 12).

Cefoxitin antagonized the activities of both cefpiramide and apalcillin against most strains of *E. cloacae* and *P. aeruginosa*. This suggests that induction of the chromosomal β -lactamase that nearly all strains of *E. cloacae*, *P. aeruginosa*, and many other species of gram-negative bacilli possess adversely affects the activities of cefpiramide and apalcillin (7, 15). In light of this, it might be anticipated that resistance to both of these antibiotics may emerge while patients are undergoing antibiotic therapy, particularly when *P. aeruginosa* or *E. cloacae* is the infecting species. This is a potential problem that cefpiramide and apalcillin share with many other β -lactam antibiotics (15).

Based on these in vitro results, a major potential application of these two new drugs would be in the treatment of infections due to *P. aeruginosa*. In addition, both agents have potential pharmacokinetic advantages. Cefpiramide has the longest half-life of any of the β -lactams tested (10) with the exception of ceftriaxone, a drug which was much less active against *P. aeruginosa* in this study. Apalcillin differs from the other extended-spectrum penicillins in that it is primarily excreted via hepatobiliary mechanisms (9). In certain settings, this may be an important consideration.

Given these characteristics, clinical evaluation of both of

these agents would appear warranted to determine whether their in vitro activities, particularly against *P. aeruginosa*, and their pharmacokinetic properties can be translated into effective therapy for specific infections.

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