Table 16.1. *In vitro* susceptibility of key bacteria to ticarcillin–clavulanate

Organism	Ticarcillin-clavulanate MIC_{90} (μg/ml) (historical data)	EUCAST MIC breakpoint (S ≤/ R >) (μg /ml)
Gram-positive bacteria		
Methicillin-susceptible *Streptococcus aureus*	0.25–1.0	S if penicillinase (+) and methicillin S
Streptococcus pneumoniae	1.25[a]	—
Streptococcus pneumoniae (penicillin MIC ≥ 2 μg/ml)	128	—
Streptococcus pyogenes	0.5[a]	—
Enterococcus faecalis	128	—
Enterococcus faecium	—	—
Listeria monocytogenes	—	—
Clostridium perfringens	0.5[a]	8/16
Gram-negative bacteria		
Escherichia coli	16–64	8/16
Haemophilus influenzae	< 0.05–0.12	IE
Klebsiella pneumoniae	4–32	8/16
Acinetobacter calcoaceticus	32	IE
Citrobacter diversus	16	8/16
Citrobacter freundii	512	8/16
Enterobacter aerogenes	128	8/16
Enterobacter cloacae	512	8/16
Proteus vulgaris	2.5	8/16
Proteus mirabilis	0.25–1	8/16
Morganella morganii	2	8/16
Providencia rettgeri	1–64	8/16
Pseudomonas aeruginosa	8–128	16/16
Serratia marcescens	64–> 128	8/16
Burkholderia cepacia	—	—
Neisseria meningitidis	0.25[a]	—
Neisseria gonorrhoeae	0.5	—
Bacteroides fragilis	0.008–8	8/16
Prevotella melaninogenica	0.1–4[a]	8/16
Stenotrophomonas maltophilia	128[b]	—

[a]Reported for ticarcillin alone.
[b]See text for details.
Abbreviations: S: susceptible; R: resistant; IE: insufficient evidence; —: no breakpoints; susceptibility testing is not recommended.
Sources: Data compiled from Knudsen *et al.* (1967); Butler *et al.* (1970); Smith *et al.* (1970); Sutherland *et al.* (1970); McCracken *et al.* (1973); Kammer *et al.* (1975); Sutter and Finegold (1976); Clarke and Zemcov (1984); Fuchs *et al.* (1984); Fass and Prior (1989); Khardori *et al.* (1990).

resistant *Staphylococcus aureus*) are important exceptions. The beta-lactamases that may be present in methicillin-susceptible *S. aureus* are readily inhibited by clavulanic acid, and these bacteria are therefore usually susceptible to ticarcillin–clavulanate (Barry, 1990). It is important that penicillin and ampicillin are more effective than ticarcillin against *E. faecalis* and *Listeria monocytogenes* and are preferred for clinical use to treat infections with these pathogens. Piperacillin–tazobactam is also usually more effective than ticarcillin–clavulanate against enterococci and may be preferable if specific treatment for this pathogen is required (Hoellman *et al.*, 1998; see Chapter 17, Piperacillin–tazobactam).

Ticarcillin is between 8 and 16 times less effective than ampicillin, penicillin, or piperacillin against those strains of *Streptococcus pneumoniae* with intermediate or high-level penicillin resistance. No increase in the efficacy of ticarcillin is achieved with the addition of clavulanic acid for these strains because the mechanism of resistance is via alteration of the penicillin-binding proteins, not production of beta-lactamase (Pankuch *et al.*, 1994; Leclercq and Duval, 1995; Pankuch *et al.*, 1995; Johnson *et al.*, 1996). This is also the case for methicillin-resistant *S. aureus* and *S. epidermidis*, in which mechanisms other than production of beta-lactamase are responsible for the antibiotic resistance.

Some interesting work has explored the possible role of ticarcillin–clavulanate as an agent to use synergistically with daptomycin for the treatment of methicillin-resistant S. *aureus* infections (Rand and Houck, 2004; Cilli *et al.*, 2006). Combinations of daptomycin plus antistaphylococcal β-lactams and daptomycin plus ceftaroline also have been