3.3.2.5 Fifth Generation

The following cephalosporins are included within this group: ceftobiprole, ceftaroline, and ceftolozane.

Ceftaroline, the active metabolite of the prodrug ceftaroline fosamil, was developed to specifically target resistant strains of bacteria, such as MRSA, and it binds with high affinity to PBP2a of staphylococci, which confers methicillin resistance, and also binds to all six PBPs in *S. pneumoniae*. Due to this capability, it shows a potent activity against MRSA and *S. pneumoniae* penicillin-resistant strains. In addition, ceftaroline has activity against enterococci, hetero-resistant vancomycin-intermediate *S. aureus* (hVISA), vancomycin-resistant *S. aureus* (VRSA), and many Gram-negative pathogens excluding extended-spectrum beta-lactamase (ESBL)-producing or AmpC-overexpressing strains. Among anaerobes, ceftaroline is active against *Propionibacterium* spp. and *Actinomyces* spp. but inactive against *B. fragilis* and *Prevotella* spp. (Bassetti et al. 2013; Shirley et al. 2013).

Ceftobiprole medocaril, another fifth-generation cephalosporin, is a prodrug that is almost completely metabolized to the active drug, ceftobiprole, following intravenous administration. It shows a broad spectrum of activity against Gram-positive and Gram-negative pathogens, similar to that of ceftaroline. Among Gram-positive pathogens, it shows activity against MRSA due to its high affinity for PBP2a, vancomycin-resistant *S. aureus*, penicillin-resistant pneumococci, and *Enterococcus faecalis*. Among Gram-negative pathogens, this drug exhibits activity against *H. influenzae* and *M. catarrhalis*, irrespective of beta-lactamase production; *P. aeruginosa*; *Acinetobacter* spp.; and non-ESBL-producing *Enterobacteriaceae*. For anaerobic bacteria, ceftobiprole is generally active against *Clostridium* spp. and *Fusobacterium* spp., but inactive against *Bacteroides* spp., *Prevotella* spp., and *Veillonella* spp. (Bassetti et al. 2013; Farrell et al. 2014).

Ceftolozane is a fifth-generation cephalosporin that differs from other cephalosporins due to its increased activity against some AmpC beta-lactamase producers including *P. aeruginosa*.

3.3.3 Monobactams

Monobactams are monocyclic beta-lactams active against Gram-negative bacilli including *Pseudomonas* spp. However, they have no activity against Gram-positive bacteria or anaerobes. Aztreonam is the only clinically available antibiotic of this group (Figure 3.5). Its activity is similar but slightly inferior to ceftazidime but can be

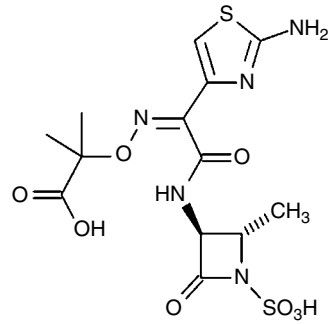

Figure 3.5 Aztreonam molecule.