More than 90% of clinical isolates from the *B. fragilis* group produce β-lactamases that are predominantly active against cephalosporins and that are highly active, cell associated, and produced constitutively. Thus, members of the *B. fragilis* group are presumed to be resistant to penicillin and ampicillin but may remain susceptible to extended-spectrum penicillins, particularly in combination with a β-lactamase inhibitor (e.g., ampicillin-sulbactam, piperacillin-tazobactam). Rates of resistance to ampicillin-sulbactam are increasing, particularly in *P. distasonis*, which has a reported resistance rate of 21% in the United States. Because β-lactamase production is not common in *Clostridium* species, these combination agents are usually effective. Of note, the newer cephalosporin/β-lactamase inhibitors (e.g., ceftolozane-tazobactam, ceftazidime-avibactam) have limited anaerobic activity.

Clindamycin is active against many anaerobes. However, rates of resistance to clindamycin among *Bacteroides* species increased in the United States from 7% in 1981 to 33% in 2010–2012. Resistance to clindamycin among non-*Bacteroides* gram-negative anaerobes is much less common (<10%). Some *Clostridium* species are resistant to clindamycin, although *C. perfringens* typically is not.

Carbapenems (ertapenem, doripenem, meropenem, and imipenem) are active against anaerobes, with fewer than 3% of *Bacteroides* isolates resistant. There is little difference among resistance rates for specific species, and, of the carbapenems, imipenem typically has the lowest resistance rate. Although the β-lactamase produced by most *Bacteroides* species is unable to inactivate carbapenems, rare *B. fragilis* strains have been reported to produce a carbapenemase.

Resistance to chloramphenicol is rare in *Bacteroides* species. Nationwide surveys in the United States have identified no resistant organisms, but some isolates with elevated minimal inhibitory concentrations (MICs)—i.e., 16 μg/mL—have been noted. Although chloramphenicol has excellent in vitro activity against all clinically relevant anaerobes, some clinical failures have been documented. Therefore, this drug may be less preferable if other active agents are available.