Table 77.1. *In vitro* spectrum of quinupristin–dalfopristin activity.

	Aerobic Gram-positive strains	Aerobic Gram-negative strains	Anaerobic strains
Susceptible	*Enterococcus faecium* *Staphylococcus aureus* Coagulase-negative staphylococci *Streptococcus agalactiae* *Streptococcus pneumoniae* *Streptococcus pyogenes*		
Intermediate	*Group C streptococcus* *Group G streptococcus*	*Haemophilus influenzae* *Legionella* spp. *Mycoplasma pneumoniae*	*Clostridium perfringens* *Peptostreptococcus* spp.
Resistant	*Enterococcus avium* *Enterococcus casseliflavus* *Enterococcus durans* *Enterococcus faecalis* *Enterococcus gallinarum* *Pediococcus* spp. *Streptococcus bovis*	Enterobacteriaceae *Haemophilus parainfluenzae* *Neisseria* spp. *Moraxella catarrhalis* *Pseudomonas* spp. *Acinetobacter* spp. *Stenotrophomonas* spp.	*Bacteroides* spp. *Clostridium* spp. *Fusobacterium* spp. *Prevotella* spp. *Veillonella* spp.

3. MECHANISM OF DRUG ACTION

Quinupristin–dalfopristin exerts antibacterial activity via inhibition of bacterial protein synthesis. Each compound binds to sequential sites located on the 50S subunit of the bacterial ribosome (Finch, 1996; Nadler *et al.,* 1999). It is thought that dalfopristin blocks attachment of the substrate to both the acceptor site and the donor site of the peptidyl transferase catalytic center, thereby inhibiting the elongation phase of ribosomal replication of Gram-positive organisms. It has further been speculated that quinupristin blocks peptide bond synthesis, which prevents the extension of polypeptide chains and promotes the detachment of incomplete protein chains. Dalfopristin exerts effects in the early stages of protein synthesis, whereas quinupristin is active in the later stages. In addition, dalfopristin binding causes a conformational change in the ribosome that subsequently increases the binding of quinupristin. The combined action of the two agents is synergistic and creates a stable drug–ribosome complex that causes inhibition of protein synthesis by several mechanisms, including prevention of peptide-chain formation, blockade of extrusion of newly formed peptide chains, and, in many instances, bacterial cell death (Cocito *et al.*; 1997; Lefebvre *et al.,* 1997a).

4. MODE OF DRUG ADMINISTRATION AND DOSAGE

Quinupristin–dalfopristin is available as an intravenous formulation only. Each single-use vial provides a total of 500 mg of sterile pyrogen-free lyophilized formulation of active drug (quinupristin, 150 mg; dalfopristin, 350 mg). The formulation should be reconstituted by slowly adding 5 ml of water with or without 5% dextrose. The vial should be then gently swirled by manual rotation without shaking to ensure dissolution of contents while limiting foam formation, and the solution should be allowed to sit for a few minutes until all the foam has disappeared. The resulting solution should be clear. The reconstituted solution should be added to 250 ml of 5% dextrose solution (approximately 2 mg/ml). An infusion volume of 100 ml may be used for central line infusions only. The desired dose should be administered by intravenous infusion (preferably via a central venous catheter) over 60 minutes. If moderate to severe venous irritation occurs

Table 77.2. Mechanisms of resistance in staphylococci and *Enterococcus faecium* to antimicrobial activity of quinupristin–dalfopristin

Mechanism of resistance	Genotype	Representative pathogens
Ribosome modification		
Constitutive MLS_B	*erm A*	Staphylococci (resistant to quinupristin only)
Drug inactivation		
Dalfopristin acetyltransferase	*vat B* or *vat; sat A*	*Staphylococcus aureus* principally CoNS, *Enterococcus faecium*
Quinupristin hydrolase	*vgb* or *vgb*-like	*E. faecium* or *S. aureus*
Active transport		
Dalfopristin efflux	*vga* or *vga*-like	CoNS principally, *E. faecium*

Abbreviations: MLS_B: macrolide–lincomycin–streptogramin B; erm: erythromycin-resistant methylase; vat: virginiamycin acetyltransferase; sat: streptogramin acetyltransferase; CoNS: coagulase-negative staphylococci; vgb: virginiamycin B; vga: virginiamycin A.
Source: Mathai *et al.,* 2001.