Quinupristin/Dalfopristin

**Antibiotic Class:**
Streptogramin

**Antimicrobial Activity:**
Gram-positive bacteria. In-vitro data suggests streptogramins possess activity against gram-negative upper respiratory tract pathogens and gram-negative anaerobes.

**Mechanism of Action:**
Inhibition of mRNA translation by binding to the 50S subunit of bacterial ribosomes.

**Pharmacodynamics:**
Predominantly independent of concentration once above four times the MIC of common Staphylococci and Streptococci.

**Pharmacokinetics:** (7.5mg/kg dose at steady state)
Cmax: 3.2 and 7.96mg/L (quinupristin and dalfopristin respectively)
Half-life: 3.07 and 1.04 hours (quinupristin and dalfopristin respectively)
Volume of distribution: 0.45 and 0.24L/kg (quinupristin and dalfopristin respectively)

**Adverse Effects:**
Venous irritation due to quinupristin/dalfopristin is common. In comparative trials approximately 40% of patients experienced infusion site adverse reactions compared to 25% of comparator treated patients. Increasing the infusion volume or administering the drug via central line may attenuate this reaction.

In two compassionate use studies, arthralgias (9.1%) and myalgias (6.6%) were the most common adverse event related to quinupristin/dalfopristin. Hyperbilirubinemia was documented in up to 25% of quinupristin/dalfopristin treated patients in compassionate use/non-comparative studies.

**Dosage:**
Intravenous only – available as 500mg (150mg quinupristin and 350mg dalfopristin) and 600mg (180mg quinupristin and 420mg dalfopristin) powder for reconstitution vials

Serious or life-threatening infections associated with vancomycin-resistant *Enterococcus faecium* – 7.5mg/kg every 8 hours
Complicated skin and skin structure infection caused by methicillin-susceptible *S. aureus* or *S. pyogenes* – 7.5mg/kg every 12 hours
Disease state based dosing:
Hepatic failure: Although no dosage official dosage adjustment recommendations exist, pharmacokinetic data in patients with hepatic cirrhosis (Childs-Pugh class A or B) suggest that dosage adjustments may be necessary.
Renal failure: No dosing adjustments are necessary in patients with renal impairment or patients undergoing peritoneal dialysis.

**Contraindications/Warnings/Precautions:**
- Therapeutic monitoring of cyclosporine levels should be performed when cyclosporine is used concomitantly with quinupristin/dalfopristin.
- Following infusion the vein should be flushed with 5% dextrose, and not saline or heparin due to incompatibility concerns.

**Drug Interactions:**
Quinupristin/dalfopristin is a potent inhibitor of the cytochrome P450 3A4 isoenzyme system. Caution should be exercised and monitoring is suggested when concomitantly administering quinupristin/dalfopristin with drugs that have narrow therapeutic windows and are substrates of the CYP3A4 substrates.

**Pregnancy:**
Category B: No evidence of risk in humans but studies inadequate.

**Brand names/Manufacturer:** Synercid/DSM pharmaceuticals (Marketed by Monarch pharmaceuticals)
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