



The Streptogramins

Quinupristin / Dalfoprisitin

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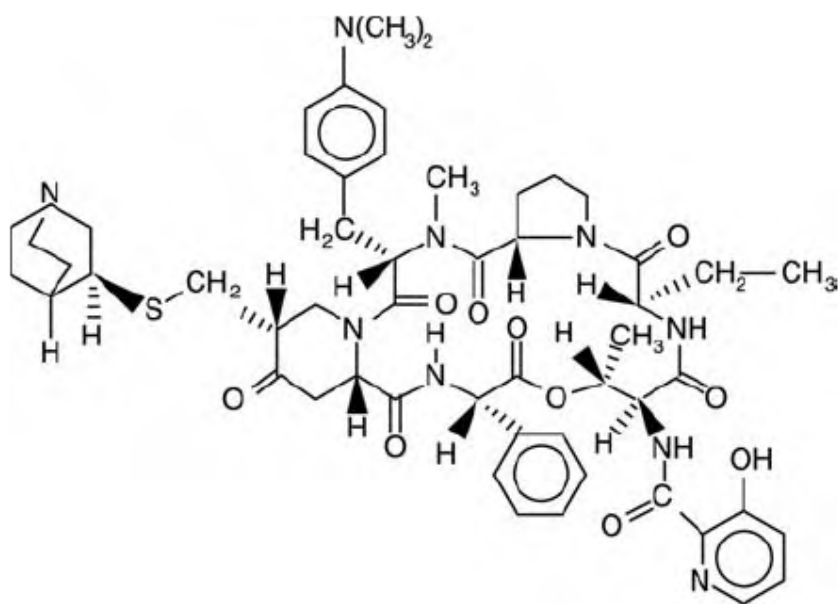
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Quinupristin-Dalfopristin (Synercid[®])

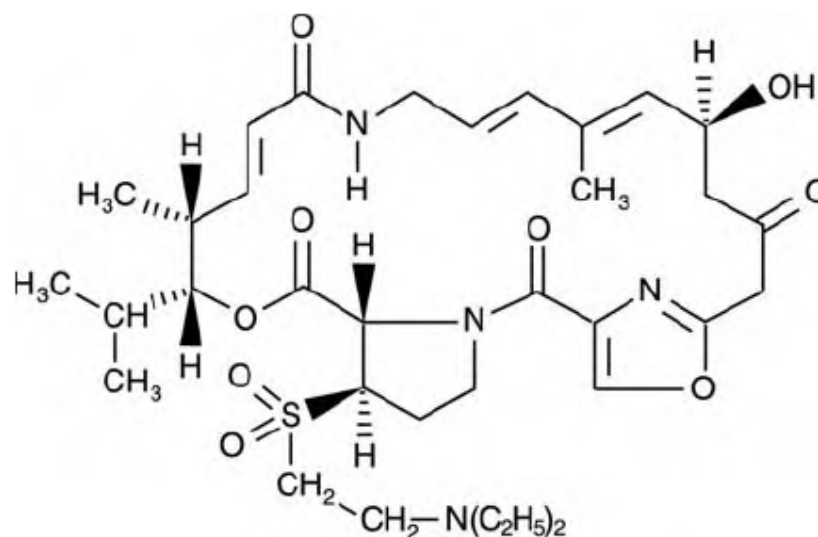


- ❑ Two streptogramin antibiotics
 - ❑ 30:70 combination
 - ❑ synergistic
- ❑ bind to different binding sites on 50S ribosome and inhibit peptide chain elongation
- ❑ Bactericidal against staphylococci but only bacteriostatic against enterococci

Quinupristin and Dalfoprisitin



Quinupristin



Dalfoprisitin



Spectrum of Activity

- ❑ ***S. aureus*, *S. epidermidis*** including methicillin resistant strains and VISA and VRSA, CNS
- ❑ **Streptococci** including penicillin-resistant pneumococci, ***S. pyogenes***
- ❑ ***E. faecium***
 - ❑ including vancomycin and aminoglycoside resistant strains with Van B phenotype
 - ❑ some strains with Van A phenotype less susceptible
- ❑ **Not** active against ***E. faecalis***
- ❑ *N. meningitidis*, *M. catarrhalis*, *L. pneumophila*, *M. pneumoniae*, *C. perfringens* & some *H. influenzae*
- ❑ *B. fragilis* variable

Resistance

3 mechanisms reported

- ❑ Methylation of the 23 S ribosomal binding site leading to MLS_B resistance (most common but dalfopristin not affected)
- ❑ Drug inactivation by acetyl-transferase or hydrolase (Staphylococci and *E. faecium*)
- ❑ Drug efflux (CNS, *E. faecium*)



Kinetics

- ❑ Only available I.V.
- ❑ Metabolized in liver and excreted in bile
- ❑ $t_{1/2}$ approximately 1 hour

Adverse Effects

- ❑ pain inflammation, edema, **thrombophlebitis** with peripheral infusion (**central line suggested**)
- ❑ **arthralgias, myalgias** common (8 - 47%) and may be severe particularly in ICU
- ❑ increased conjugated bilirubin



Drug Interactions

- ❑ Potent inhibitor of **CYP3A4**
- ❑ increased serum levels of
 - ❑ nifedipine, verapamil,
 - ❑ HMG CoA reductase inhibitors
 - ❑ diazepam, midazolam,
 - ❑ cyclosporine, tacrolimus,
 - ❑ most protease inhibitors,
 - ❑ quinidine, lidocaine, disopyramide

Indications

- ❑ Bacteremia and life threatening infections caused by *E. faecium* resistant to Vancomycin
- ❑ Complicated skin and skin structure infections caused by *S. aureus* (MRSA) and *S. epidermidis* (MRSE), *S. pyogenes*
- ❑ In 90 patients with bone & joint infections and SSTIs MRSA success rate 71.1%
- ❑ 396 patients with *E. faecium* 70.5% clinical response, 65.8% overall success rate