

Daptomycin

Antibiotic Class:

Lipopeptide

Antimicrobial Spectrum:

Gram-positive bacteria.

Mechanism of Action:

Calcium-dependent binding/insertion of the lipophilic tail into gram-positive cytoplasmic membrane. Oligomerization/channel formation occurs with subsequent ion leakage and collapse of organism leading to cell death. (Figure 2)

Pharmacodynamics:

AUC/MIC ratio predictive of pharmacodynamic activity.

Pharmacokinetics: (4mg/kg dose)

Cmax: 77.5mg/L; Half-life: 8 hours; Volume of distribution: 7L; Clearance (total): 8ml/h/kg

Adverse Effects:

The most common adverse effects from this study were constipation (6.2%), nausea (5.8%), injection site reaction (5.8%) and headache (5.4%).

Dosage:

Intravenous only – available as 500 mg vials (powder for reconstitution)

Complicated skin and soft tissue infection – 4mg/kg every 24 hours

Doses studied in ongoing clinical trials for endocarditis and bacteremia are 6mg/kg every 24 hours

Disease state based dosing:

Hepatic failure: Not significantly altered in patients with hepatic impairment; no dosage adjustments in this population are necessary

Renal failure: In patients with an estimated CrCl < 40ml/min require a dosage adjustment of 4mg/kg every 48 hours.

Dosing during Continuous Renal Replacement Therapy

CVVH (Continuous venovenous hemofiltration): 4 or 6mg/kg IV q48h

CVVHD (Continuous venovenous hemodialysis): 4 or 6mg/kg IV q48h

CVVHDF (Continuous venovenous hemodiafiltration) 4 or 6mg/kg IV q48h

Note: CVVH is mainly for fluid removal alone. Many institutions will employ more CVVHD or CVVHDF which combine dialysis with fluid removal.

Contraindications/Warnings/Precautions:

- Patients receiving daptomycin should be monitored for the development of muscle pain or weakness.
- Consideration should be given to temporarily suspending agents associated with rhabdomyolysis.

Drug Interactions:

Limited data available.

Pregnancy:

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

Monitoring Requirements:

CPK levels should be monitored weekly. Daptomycin should be discontinued in patients with unexplained signs and symptoms of myopathy in conjunction with CPK elevation > 1000U/L, or in patients without reported symptoms who have marked elevations in CPK (>2000U/L).

Brand names/Manufacturer: Cubicin/Cubist pharmaceuticals