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Daptomycin

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1. DESCRIPTION

Daptomycin (Cubicin) (formerly LY 146032) is the first in the new antibiotic class of the cyclic lipopeptides. Daptomycin is more active *in vitro* than glycopeptides against a wide range of Gram-positive aerobic as well as anaerobic organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE). The initial development program started in the 1980s was terminated owing to treatment failures in endocarditis with 2 mg/kg and the occurrence of potential drug-induced myopathy. With the increasing prevalence of resistant Gram-positive microorganisms, in particular MRSA, clinical development of daptomycin was reinstigated in 1997 by evaluating once-daily dosing regimens. The official dosage recommendations are 4 mg/kg or 6 mg/kg once daily; however, currently much higher doses are used in clinical practice.

Daptomycin is derived from *Streptomyces roseosporus*. It is a cyclic lipopeptide comprising 13 amino acids with a water-soluble hydrophilic core and a lipophilic tail. The chemical formula is $C_{72}H_{101}N_{17}O_{26}$, and the molecular weight is large, 1620.67. The chemical structure of daptomycin is shown in Figure 45.1.

The mechanism of action depends on a fast depolarization of the bacterial cytoplasmic membrane, resulting in a rapid concentration-dependent bactericidal effect. Daptomycin is available for i.v. use only.

2. ANTIMICROBIAL ACTIVITY

2a. Routine susceptibility

Daptomycin is active against Gram-positive organisms only. It can be used in combination with other antibiotics to obtain

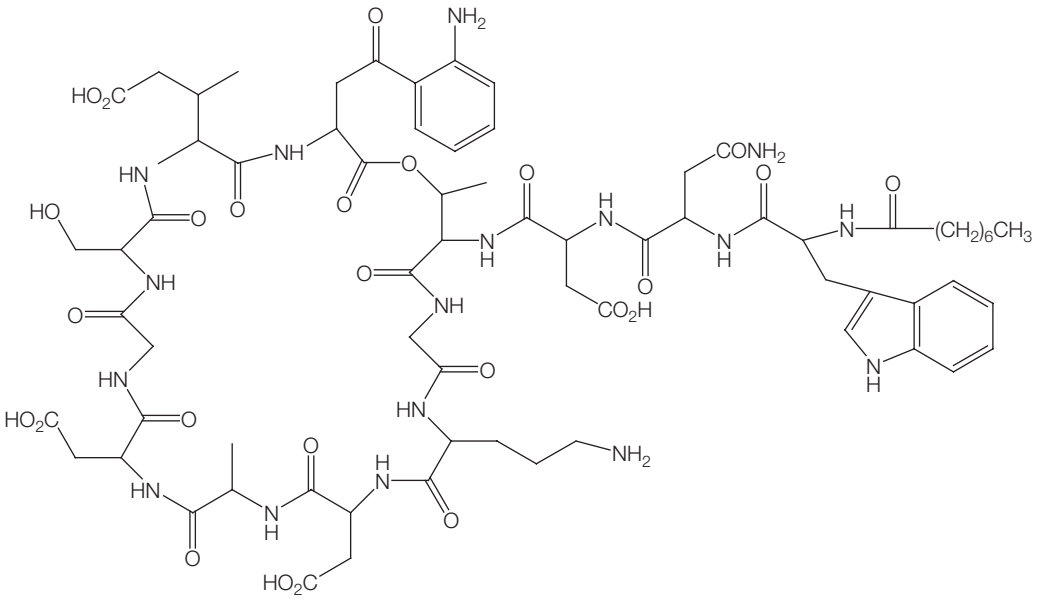

Figure 45.1. Chemical structure of daptomycin.