

# Patent Protection Guide: CUBICIN®



## About CUBICIN® (daptomycin for injection)

CUBICIN®, developed and launched by Cubist, is the only once-daily I.V. bactericidal antibiotic approved in the U.S. (at 4 mg/kg) for the treatment of complicated skin and skin structure infections caused by susceptible strains of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-resistant strains, also known as MRSA), *Streptococcus pyogenes*, *S. agalactiae*, *S. dysgalactiae subsp equisimilis* and *Enterococcus faecalis* (vancomycin-susceptible strains only).

CUBICIN is also approved in the U.S., at 6 mg/kg, for the treatment of *S. aureus* bloodstream infections (bacteremia), including right-sided infective endocarditis caused by MRSA and MSSA. CUBICIN is the only I.V. antibiotic approved for this indication based on the results of a prospective, randomized, controlled registration trial.

## Significance of Cubist's Dosing Discovery (The Dosing Patents)

Daptomycin was discovered and first developed by scientists at Eli Lilly and Co. In early studies, the drug showed promise as an antibiotic to treat Gram-positive infections. However, when scientists at Eli Lilly attempted to administer to subjects amounts of daptomycin necessary to treat serious infections, they encountered unacceptable levels of skeletal muscle toxicity and discontinued development of daptomycin.

In 1997, Cubist licensed exclusive worldwide rights to daptomycin from Eli Lilly and initially planned to develop the drug for topical administration, to avoid the toxicity previously encountered. Discoveries by Cubist scientists revealed that toxicity could be minimized if a higher dose of daptomycin was administered once a day. This unexpected discovery is the basis of two “method of administration” patents which are listed in the Orange Book and led Cubist to develop the drug for serious infections.

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## **CUBICIN is protected by five patents listed in the FDA Orange Book**

The FDA Orange Book-listed patents for CUBICIN are U.S. Patent Nos. RE 39,071; 6,468,967; 6,852,689; 8,003,673 and 8,058,238 (the '071, '967, '689, '673 and '238 patents, respectively).

### **1. U.S. Patent No. RE 39,071 (composition with less than certain levels of impurities)**

The '071 patent, entitled "Anhydro- and Isomer-A-21978C Cyclic Peptides," covers the pharmaceutical composition of daptomycin sold in the CUBICIN vial. The '071 patent claims daptomycin compositions with two specific impurities found in daptomycin at a combined total level of less than 6% by weight. The '071 patent also claims methods of using these purified pharmaceutical compositions to treat bacterial infections. This patent, which is a reissue of U.S. Patent No. 5,912,226, will expire on June 15, 2016.

### **2. U.S. Patent No. 6,468,967 (method of administration) (one of the Dosing Patents)**

The '967 patent, entitled "Methods for Administration of Antibiotics," covers methods of administering daptomycin at a dosage interval that minimizes skeletal muscle toxicity. The claimed methods involve treating a human patient anywhere from once every 24 hours to once every 48 hours with 3 -75 mg of daptomycin per kilogram of the patient's body weight. The '967 patent also covers the co-administration of any other antibiotic with daptomycin in this dosing regimen. This patent will expire on September 24, 2019.

### **3. U.S. Patent No. 6,852,689 (method of administration) (one of the Dosing Patents)**

The '689 patent, entitled "Methods for Administration of Antibiotics," is a continuation of the '967 patent. The '689 patent covers methods of administering daptomycin at a dosage interval that minimizes skeletal muscle toxicity. The claimed methods involve treating a human patient anywhere from once every 48 hours to once weekly with at least 3 mg of daptomycin per kilogram of the patient's body weight. The '689 patent also claims the co-administration of any other antibiotic with daptomycin in this dosing regimen. The '689 patent (like the '967 patent) will expire on September 24, 2019.

### **4. U.S. Patent No. 8,003,673 (method of treatment)**

The '673 patent, entitled "Daptomycin for the Treatment of Biofilm and Catheter Salvage" covers methods of treating infections with daptomycin. For example, claim 1

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covers “[a] method for treating a biofilm, comprising providing a solution of daptomycin in a lactated Ringer’s solution to a biofilm.” The ’673 patent will expire on September 4, 2028.

## **5. U.S. Patent No. 8,058,238 (high purity daptomycin composition)**

The ’238 patent, entitled “High Purity Lipopeptides,” covers compositions of daptomycin obtained by certain processes and having greater than or about 93% purity relative to fourteen specific impurities found in daptomycin. The ’238 patent covers the product sold in the CUBICIN vial and will expire on November 28, 2020.

**Helpful links:** [FDA Electronic Orange Book--daptomycin page](#)

## **Additional Patents Relating to CUBICIN**

Cubist also owns a patent covering methods of purifying daptomycin. There are also other pending patent applications related to CUBICIN.

- **U.S. Patent No. 6,696,412 (methods of purifying daptomycin)**

The ’412 patent, entitled “High Purity Lipopeptides, Lipopeptide Micelles and Processes for Preparing Same,” claims methods of purifying daptomycin. These methods can provide daptomycin of at least 98% purity, and can render the compound essentially free of fourteen different impurities. The ’412 patent will expire on November 28, 2020. Patents for methods of manufacturing a pharmaceutical are not listed in the Orange Book.

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