



NDA 21-572/S-008

Cubist Pharmaceuticals, Inc.
Attention: Francis P. Tally, MD
Senior Vice President and Chief Scientific Officer
65 Hayden Avenue
Lexington, MA 02421

Dear Dr. Tally:

Please refer to your supplemental new drug application dated September 22, 2005, received September 26, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CUBICIN[®] (daptomycin for injection) Intravenous, 500 mg/vial.

We also acknowledge receipt of your submissions dated October 24, 2005, November 14, 2005, November 16, 2005, December 22, 2005, December 28, 2005, January 3, 2006, January 19, 2006, January 23, 2006, January 24, 2006 (2), January 25, 2006 (2), January 26, 2006 (2), January 31, 2006, February 3, 2006, February 10, 2006, February 21, 2006, February 22, 2006 (2), February 24, 2006 (2), February 28, 2006, March 1, 2006, March 3, 2006, March 13, 2006 (2), March 15, 2006, March 22, 2006, and March 27, 2006.

Your submissions of April 14, 2006, April 18, 2006, April 19, 2006, April 20, 2006, May 18, 2006, May 22, 2006 and May 24, 2006 constituted a complete response to our March 24, 2006 action letter.

This supplemental new drug application provides for the use of CUBICIN[®] (daptomycin for injection) Intravenous, 500 mg/vial, for the treatment of *Staphylococcus aureus* bloodstream infections (bacteremia), including those with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates.

We completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission “**FPL for approved NDA 21-572/S-008.**” Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 0 to 18 years until December 31, 2011.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed as follows:

1. Deferred pediatric study under PREA for the treatment of *Staphylococcus aureus* bloodstream infections (bacteremia), including those with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates.

Final Report Submission: December 31, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated “**Required Pediatric Study Commitments**”.

We also remind you of your postmarketing study commitments, in your submission dated May 25, 2006. These commitments are listed below:

Clinical:

1. Description of Commitment: Conduct a study to evaluate the potential impact of daptomycin used in combination therapy in the treatment of *S.aureus* infective endocarditis.

Protocol Submission:	by	November, 2006
Study Start	by	April, 2007
Final Report Submission	by	June, 2010

Microbiology:

2. Description of Commitment: Perform studies to assess penetration of daptomycin into vegetations using simulated endocarditis vegetations *in vitro* and in animals.

Protocol Submission:	by	September, 2006
Study Start	by	October, 2006
Final Report Submission	by	December, 2007

3. Description of Commitment: Perform *in vitro* studies to evaluate potential factors affecting daptomycin potency including vancomycin exposure and the susceptibility of vancomycin intermediate *S. aureus* (VISA) strains to daptomycin.

Protocol Submission: by July, 2006
Study Start by August, 2006
Final Report Submission by December, 2006

4. Description of Commitment: Perform studies of the activity and penetration of daptomycin in biofilms.

Protocol Submission: by September, 2006
Study Start by December, 2006
Final Report Submission by April, 2007

5. Description of Commitment: Evaluate the efficacy of daptomycin in combination with other antibiotics *in vitro* and in animal models of bacterial endocarditis.

Protocol Submission: by September, 2006
Study Start by October, 2006
Final Report Submission by December, 2007

We also remind you that you have agreed to collect the following information:

Clinical:

1. Monitor outcomes of patients with *S. aureus* bacteremia and infective endocarditis from the ongoing Cubicin Outcome Registry and Experience (CORE) database. Summarize data in annual report for 2 years.

Microbiology:

1. Monitor reports of resistance and collect isolates for determination of daptomycin and vancomycin minimum inhibitory concentration (MIC) when possible. Submit findings in periodic safety update reports (PSUR).
2. Perform surveillance studies to monitor the activity of daptomycin for a period of no less than 2 years. A summary of findings are to be included in each year's annual report.
3. Collect organisms that become resistant to daptomycin and perform studies to characterize the mode(s) of resistance, including genetic changes.
4. Determine cross-resistance of daptomycin resistant bacteria to other antimicrobials.
5. Evaluate the impact of sub-inhibitory concentrations of daptomycin on the development of resistance and the results of serial passage experiments.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **“Postmarketing Study Commitment Protocol”**, **“Postmarketing Study Commitment Final Report”**, or **“Postmarketing Study Commitment Correspondence.”**

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call J. Christopher Davi, Regulatory Project Manager at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director,
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Approved labeling dated May 25, 2006

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Janice Soreth
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