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RESEARCH**

*APPLICATION NUMBER:*  
**200327**

**APPROVAL LETTER**



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 200327

**NDA APPROVAL**

Cerexa, Inc.  
Attention: Bruce Lu, R.Ph., RAC  
Senior Director, Regulatory Affairs  
2100 Franklin St., Suite 900  
Oakland, CA 94612

Dear Mr. Lu:

Please refer to your New Drug Application (NDA) dated December 29, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Teflaro (ceftaroline fosamil) for Injection.

We acknowledge receipt of your amendments dated January 8, 20, 26 and 29; February 2 and 4, April 14, 23(2), 28, 29 and 30; May 3 and 14; June 2, 7, 18, 21 and 23; July 2, 9, 13, 14, 20 and 27; August 2(2), 4, 6, 9, 10, 18, 19, 20, 24 and 30; September 16, 20, 21 and 24; and October 13(2), 14, 18(2), 20 and 28(2), 2010.

This new drug application provides for the use of Teflaro (ceftaroline fosamil) for Injection for the treatment of Acute Bacterial Skin and Skin Structure Infections and Community Acquired Bacterial Pneumonia.

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

**LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

## **CARTON AND IMMEDIATE CONTAINER LABELS**

We acknowledge your October 14, 2010 submission containing carton and container labels.

Submit final printed carton and container labels that are identical to the carton labels submitted on October 14, 2010 and the immediate container labels submitted on October 20, 2010 as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).” Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 200327**”. Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indications in pediatric patients unless this requirement is waived, deferred or inapplicable.

We are deferring submission of pediatric trials in patients aged 0 to 17 years for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) and Community-Acquired Bacterial Pneumonia (CABP) until July 2015, because this product is ready for approval for use in adults and pediatric trials have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below:

### **1692-001: Single dose pharmacokinetic trial**

Perform a trial in pediatric patients being treated concomitantly with antibacterial agent(s) to evaluate single dose pharmacokinetic parameters and assess safety of Teflaro (ceftaroline fosamil) in all pediatric age groups. Five age cohorts must be studied as follows:

- Group 1: children from 6 to less than 12 years
- Group 2: children from 24 months to less than 6 years
- Group 3: infants/toddlers from 28 days to less than 24 months

- Group 4: term neonates less than 28 days; (stratification within the group: 0-14 days; >14 days to <28 days)
- Group 5: pre-term neonates less than 28 days (stratification within the group: 0-14 days; >14 days to <28 days)

There must be a minimum of 8 evaluable subjects per cohort. In Group 3, there will be an equal representation of patients aged 28 days to <12 months and  $\geq$ 12 months to <24 months.

Final Protocol Submission: 11/2010  
Trial Completion Date: 01/2014  
Final Report Submission: 07/2014

**1692-002:** Perform a randomized comparison of Teflaro (ceftaroline fosamil) and comparator in pediatric subjects with CABP utilizing an enrichment strategy for enrollment of patients with methicillin-resistant *Staphylococcus aureus* (MRSA). Pediatric patients under 17 years of age with CABP must be enrolled, with a minimum of 150 patients receiving Teflaro (ceftaroline fosamil).

Final Protocol Submission: 09/2011  
Trial Completion Date: 05/2014  
Final Report Submission: 11/2014

**1692-003:** Perform a randomized comparison of Teflaro (ceftaroline fosamil) and comparator in pediatric subjects with ABSSSI including patients with infection suspected or demonstrated to be caused by MRSA. Pediatric patients under 17 years of age with ABSSSI must be enrolled, with a minimum of 150 patients receiving Teflaro (ceftaroline fosamil).

Final Protocol Submission: 09/2011  
Trial Completion Date: 05/2014  
Final Report Submission: 11/2014

**1692-004: Cerebrospinal Fluid (CSF) Concentration Trial**

Perform a trial assessing the CSF concentration profile of Teflaro (ceftaroline fosamil) in infants < 2 months of age. A minimum of 12 infants < 2 months of age receiving antibacterials for treatment of late-onset neonatal sepsis must be studied.

Final Protocol Submission: 05/2014  
Trial Completion Date: 09/2016  
Final Report Submission: 03/2017

**1692-005:** Perform a randomized comparison of Teflaro (ceftaroline fosamil) and comparator in infants < 2 months of age with ABSSSI and CABP including patients with infections suspected or demonstrated to be caused by MRSA.

Final Protocol Submission: 05/2014  
Trial Completion Date: 09/2016  
Final Report Submission: 03/2017

Submit final reports to the NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated “**Required Pediatric Assessments**”.

### **POSTMARKETING REQUIREMENTS UNDER 505(o)**

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the signal of serious risk of development of bacterial resistance.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required, to conduct the following:

**1692-006:** Conduct a prospective study over a five-year period after introduction of Teflaro (ceftaroline fosamil) to the market to determine if decreased susceptibility to Teflaro (ceftaroline fosamil) is occurring in the target bacteria included in the Indications section of the approved Teflaro (ceftaroline fosamil) package insert. Provide a detailed protocol describing the study to the Agency for review and comment before commencing the study.

The timetable you submitted on October 14, 2010 states that you will conduct this study according to the following schedule:

Final Protocol Submission: 01/2011  
First Interim Report: 10/2011, and then annually until 10/2015  
Study Completion: 04/2016  
Final Report Submission: 10/2016

Submit the protocol to your IND 71,371, with a cross-reference letter to this NDA. Submit all interim and final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate

**“Required Postmarketing Protocol Under 505(o)”, “Required Postmarketing Final Report Under 505(o)”, “Required Postmarketing Correspondence Under 505(o)”.**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

**POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitment in your submission dated October 14, 2010. This commitment is listed below:

**1692-007:** Conduct a prospective, randomized trial evaluating the efficacy and safety of Teflaro (ceftaroline fosamil) versus comparator in the treatment of patients with CABP at high risk for infection caused by MRSA.

Final Protocol Submission: 10/2011  
Trial Completion Date: 09/2016  
Final Report Submission: 04/2017

Submit clinical protocols to your IND 71,371 for this product. Submit nonclinical and chemistry, manufacturing, and control protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(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 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/trial, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,”** or **“Postmarketing Commitment Correspondence.”**

## **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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

## **LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program  
Office of Special Health Issues  
Food and Drug Administration  
10903 New Hampshire Ave  
Building 32, Mail Stop 5353  
Silver Spring, MD 20993

## **REPORTING REQUIREMENTS**

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

## **MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

New molecular entities and new biologics qualify for a post-action feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Carmen DeBellas, Regulatory Project Manager, at (301) 796-1203.

Sincerely,

*{See appended electronic signature page}*

Edward M. Cox, MD., MPH  
Director  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

ENCLOSURES:  
Content of Labeling



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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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EDWARD M COX  
10/29/2010