DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206494/S-002

SUPPLEMENT APPROVAL

Cerexa, Inc.
A Subsidiary of Forest Laboratories, (LLC)
Attention: Amjad Iqbal, PharmD
Senior Director, Regulatory Affairs
Harborside Financial Center
Plaza V, Suite 1900
Jersey City, NJ 07311

Dear Dr. Iqbal:

Please refer to your Supplemental New Drug Application (sNDA) dated December 22, 2015, received December 22, 2015, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Avycaz (ceftazidime and avibactam) for Injection.

This Prior Approval supplemental new drug application provides for a revision to the Indications and Usage Section (1) to remove the following statement under Complicated Intra-Abdominal Infections (cIAI):

"As only limited clinical safety and efficacy data for AVYCAZ are currently available, reserve AVYCAZ for use in patients who have limited or no alternative treatment options."

In addition, this sNDA provides for updates to the Adverse Reactions (6) and Clinical Studies (14.1) sections to include clinical data from the Phase 3 cIAI trial, and an update to the Microbiology subsection (12.4), to revise the disk diffusion interpretive criteria for *Pseudomonas aeruginosa*.

APPROVAL & LABELING

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

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf
The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENT

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 indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We remind you of your previous PREA post-marketing requirements (PMRs) specified in our February 25, 2015, original NDA approval letter. We note that the following three studies will evaluate the use of Avycaz (ceftazidime and avibactam) in children:

- 2862-1 Conduct a randomized multicenter, active-controlled trial to evaluate the safety and tolerability of AVYCAZ (ceftazidime and avibactam) in children from 3 months to less than 18 years of age with cUTI. The dose for this study will be determined upon review of the data to be submitted by June 2015 from a single-dose, multicenter, non-comparative study assessing the pharmacokinetics of AVYCAZ (ceftazidime and avibactam) in pediatric patients from 3 months to less than 18 years of age.

The timetable you submitted on February 11, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 06/2015
Study Completion: 09/2017
Final Report Submission: 09/2018

- 2862-2 Conduct a randomized, multicenter, active-controlled trial to evaluate the safety and tolerability of AVYCAZ (ceftazidime and avibactam) in children from 3 months to less than 18 years of age with cIAI. The dose for this study will be determined upon review of the data to be submitted by June 2015 from a single-dose, multicenter, non-comparative study assessing the pharmacokinetics of AVYCAZ (ceftazidime andavibactam) in pediatric patients from 3 months to less than 18 years of age.

The timetable you submitted on February 11, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 06/2015
Study Completion: 09/2017
Final Report Submission: 09/2018

- 2862-3 Conduct a trial to evaluate the pharmacokinetics, safety and tolerability of AVYCAZ (ceftazidime and avibactam) in children from birth to less than 3 months of age with late-onset sepsis.

The timetable you submitted on February 11, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 06/2018
Study Completion: 12/2019
Final Report Submission: 12/2020

Submit the protocols to your IND 101307 with a cross-reference letter to NDA 206494.

Reports of these required pediatric post-marketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies.
When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

We also remind you that there are other post-marketing requirements and post-marketing commitments listed in our February 26, 2015, approval letter that are still open.

REPORTING REQUIREMENTS

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 Carmen DeBellas, Regulatory Project Manager, at (301) 796 1203.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

SUMATHI NAMBIAR
06/22/2016