



NDA 206494/S-003

SUPPLEMENT APPROVAL

Cerexa, Inc. (A Subsidiary of Forest Laboratories, LLC)
Attention: Amjad Iqbal, PharmD
Executive Director, Regulatory Affairs
Harborside Financial Center, Plaza 5
185 Hudson Street, Suite 1900
Jersey City, NJ 07311

Dear Dr. Iqbal:

Please refer to your Supplemental New Drug Application (sNDA) dated July 28, 2016, received July 28, 2016, and your amendments, submitted 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 revisions to the **INDICATIONS AND USAGE** section to remove the following statement under **Complicated Urinary Tract Infections (cUTI), including Pyelonephritis** in the **HIGHLIGHTS** and **FULL PRESCRIBING INFORMATION**:

“In the treatment of cUTI, as only limited clinical safety and efficacy data for AVYCAZ are currently available, reserve AVYCAZ for use in patients with cUTI who have limited or no alternative treatment options.”

In addition, this supplemental new drug application provides for revisions to the following sections/subsections of labeling to include data from the cUTI trials:

- **WARNINGS AND PRECAUTIONS (5)** section
- **ADVERSE REACTIONS (6)** section
- **USE IN SPECIFIC POPULATIONS (8)** section/**Geriatric Use (8.5)** subsection
- **CLINICAL PHARMACOLOGY (12)** section/**Microbiology (12.4)** subsection
- **CLINICAL STUDIES (14)** section/**Complicated Urinary Tract Infections (cUTI), including Pyelonephritis (14.2)** subsection

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.

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

We remind you of your required post-marketing studies (PMRs) as specified in the February 25, 2015, NDA approval letter. These 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, noncomparative study assessing the pharmacokinetics of AVYCAZ (ceftazidime and avibactam) in pediatric patients from 3 months to less than 18 years of age.

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, noncomparative study assessing the pharmacokinetics of AVYCAZ (ceftazidime and avibactam) in pediatric patients from 3 months to less than 18 years of age.

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.

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

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, please contact Carmen DeBellas, Chief, Project Management Staff, 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
01/26/2017