NDA 217906

NDA APPROVAL

AbbVie, Inc.
Attention: Linda Kunka, MA
Director, Regulatory Affairs
100 Park Avenue
Florham Park, NJ 07932

Dear Linda Kunka:

Please refer to your new drug application (NDA) dated and received, August 9, 2024, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Emblaveo (aztreonam and avibactam) for injection.

This NDA provides for the use of Emblaveo as follows:

Emblaveo, in combination with metronidazole, is indicated in patients 18 years and older who have limited or no alternative options for the treatment of complicated intra-abdominal infections (cIAI) including those caused by the following susceptible gram-negative microorganisms: *Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Enterobacter cloacae complex, Citrobacter freundii complex,* and *Serratia marcescens*. Approval of this indication is based on limited clinical safety and efficacy data for Emblaveo.

APPROVAL & LABELING

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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

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

FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information) 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 *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 217906**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Emblaveo (aztreonam and avibactam) for injection shall be 24 months from the date of manufacture when stored at 2°C to 8°C (36°F to 46°F).

MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Deborah Kim, PharmD, RAC
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6349
10903 New Hampshire Avenue
Silver Spring, Maryland
Use zip code **20903** *if shipping via United States Postal Service (USPS).*
Use zip code **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

ADVISORY COMMITTEE

Your application for Emblaveo was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages birth to less than 18 years, because this product is ready for approval for use in adults and the pediatric studies 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)(4)(C) of the Federal Food, Drug, and Cosmetic Act/FDCA. These required studies are listed below.

4778-1 Conduct a multiple-dose, open-label (with a blinded observer), comparator controlled study to evaluate the pharmacokinetics, safety, and tolerability of aztreonam-avibactam for injection in patients aged 9 months and older to less than 18 years who are hospitalized due to complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), hospital-acquired bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VABP), or bloodstream infections (BSI) caused by gram-negative organisms (confirmed or suspected).

Final Protocol Submission: Submitted
Study Completion: 03/2026
Final Report Submission: 08/2026

For this study, at least 12 to 15 of the randomized patients will have a cIAI diagnosis.

4778-2 Conduct a two-part, open-label study enrolling neonates and infants from birth to less than 9 months of age to evaluate the pharmacokinetics, safety, and tolerability of aztreonam-avibactam for injection.

Final Protocol Submission: Submitted

Study Completion: 09/2027
Final Report Submission: 02/2028

The first part of the study should be a single-dose PK study enrolling neonates and infants from birth to less than 9 months of age who are hospitalized with bacterial infections requiring intravenous antibacterial therapy. The second part of the study should be an open-label, multiple-dose, single arm study enrolling neonates and young infants aged birth to less than 9 months who are hospitalized with gram-negative bacterial infections requiring intravenous antibacterial therapy.

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocol(s) to your IND 115969, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an 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.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (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 a signal of a serious risk of developing resistance to bacterial pathogens specific to the indication in the labeling.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

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

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

4778-3 Conduct a U.S. surveillance study over a five-year period after the introduction of aztreonam-avibactam to the market to determine if resistance or decreased susceptibility to aztreonam-avibactam is occurring in the target population of bacteria identified in the approved aztreonam-avibactam label.

The timetable you submitted on January 8, 2025, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2025
First Interim Report:	05/2026
Second Interim Report:	05/2027
Third Interim Report:	05/2028
Fourth Interim Report:	05/2029
Fifth Interim Report:	05/2030
Study Completion:	02/2030
Final Report Submission:	12/2030

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit clinical protocol(s) to your IND 115969 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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(a)(1) 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(a)(1) 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

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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 NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4778-4 Conduct studies to develop a validated analytical procedure for the quantification of [redacted] (b) (4) and to establish an appropriate acceptance criterion for the [redacted] (b) (4) specification.

The timetable you submitted on January 23, 2025, states that you will conduct this study according to the following schedule:

Interim Report: 12/2025
Final Report: 09/2026

The final report should be submitted as a prior approval supplement. The final report submission should be identified as "Final Report Submission for PMC 4778-4 in addition to being identified as a "Prior Approval Supplement".

4778-5 Conduct method validation studies for the analytical procedure used for the determination of the [redacted] (b) (4) impurity in the drug product.

The timetable you submitted on January 23, 2025, states that you will conduct this study according to the following schedule:

Final Report: 06/2025

The final report should be submitted as a prior approval supplement. The final report submission should be identified as "Final Report Submission for PMC 4778-5 in addition to being identified as a "Prior Approval Supplement".

4778-6 Conduct method validation studies for the analytical procedure used for the determination of [redacted] (b) (4) impurity in the drug product.

The timetable you submitted on January 23, 2025, states that you will conduct this study according to the following schedule:

Interim Report: 12/2025
Final Report: 09/2026

The final report should be submitted as a prior approval supplement. The final report submission should be identified as "Final Report Submission for PMC 4778-6 in addition to being identified as a "Prior Approval Supplement".

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[5]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

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

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website[8].

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[8] https://www.uspnf.com/

If you have any questions, contact Deborah Kim, PharmD, RAC, Senior Regulatory Project Manager, at (301) 796-9053 or Deborah.Wang@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Peter Kim, MD, MS
Director
Division of Anti-Infectives
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

PETER W KIM
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