NDA 215960

NDA APPROVAL

GlaxoSmithKline LLC (GSK)
Attention: Angela Natilla, PhD
Director, Global Regulatory Strategy
2000 Tower Oaks Boulevard, Suite 360
Rockville, MD 20852

Dear Dr. Natilla:

Please refer to your new drug application (NDA) received October 27, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Utebzi (tebipenem pivoxil) tablets.

We acknowledge receipt of your amendment dated December 18, 2025, which constituted a complete response to our June 24, 2022, action letter.

This NDA provides for the use of Utebzi (tebipenem pivoxil) tablets, for oral use, for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by designated susceptible microorganisms in adult patients who have limited or no alternative oral treatment options.

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 and Patient Package Insert) as well as annual reportable

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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 IMMEDIATE CONTAINER LABELING

Submit final printed carton and immediate container labeling that are identical to the enclosed carton and immediate 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 215960**." 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 Utebzi (tebipenem pivoxil) tablets shall be 24 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F), brief excursions permitted between 15°C to 30°C (59°F to 86°F).

MARKET PACKAGE

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

Deborah Kim
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).*

[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 Utebzi 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 waiving the pediatric study requirement for ages from birth to less than 2 months because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group. In patients from birth to less than 2 months, UTIs are frequently associated with systemic infection necessitating intravenous therapy and oral therapy is generally not appropriate.

We are deferring submission of your pediatric study for ages 2 months to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. This required study is listed below.

5007-1 Conduct an open-label, single arm, non-comparative study to evaluate the pharmacokinetics, safety, and tolerability of multiple doses of tebipenem pivoxil in pediatric patients from 2 months to less than 18 years of age with complicated urinary tract infections, including pyelonephritis.

Draft Protocol Submission:	08/2027
Final Protocol Submission:	01/2028
Study Completion:	01/2033
Final Report Submission:	07/2033

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. See guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act.*

Submit the protocol to your IND 132744, with a cross-reference letter to this NDA. Reports of this required pediatric postmarketing study 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 this study. 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 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 identify an unexpected serious risk of the potential presence of tebipenem in human breast milk resulting in effects on the breastfed infant, to identify an unexpected serious risk of adverse maternal, fetal, and infant outcomes resulting from the use of tebipenem during pregnancy, and to assess a signal of a serious risk of the development of drug resistance to tebipenem.

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 these serious risks.

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

5007-2 Perform a lactation study in lactating women who have received tebipenem pivoxil to measure concentrations of tebipenem, its major metabolites, and pivalate in breast milk using a validated assay. Assess the effects on the breastfed infant, if available, based on study population.

The timetable you submitted on June 2, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	01/2027
Final Protocol Submission:	07/2027
Study Completion:	07/2029
Final Report Submission:	01/2030

5007-3 Conduct a worldwide descriptive study that collects prospective and retrospective data in women exposed to Utebzi during pregnancy to assess risk of pregnancy and maternal complications, and adverse effects on the developing fetus, neonate, and infant, specifically neonatal hypocarnitinemia.

The timetable you submitted on June 5, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol submission:	01/2027
Final Protocol Submission:	07/2027
First Interim Report:	07/2030
Second Interim Report:	07/2033
Study Completion:	07/2037
Final Report Submission:	01/2038

For the pregnancy study, assess infant outcomes through at least the first year of life. The minimum number of patients will be specified in the protocol.

5007-4 Conduct a U.S. surveillance study over a five-year period after the introduction of Utebzi (tebipenem pivoxil) oral tablets to the market to determine if resistance or decreased susceptibility to tebipenem is occurring in the target population of bacteria that are in the approved Utebzi label.

The timetable you submitted on May 21, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	08/2026
Final Protocol Submission:	12/2026
First Interim Report:	12/2027
Second Interim Report:	12/2028
Third Interim Report:	12/2029
Fourth Interim Report:	12/2030
Fifth Interim Report:	12/2031
Study Completion:	09/2032
Final Report Submission:	12/2032

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]

[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.

Submit clinical protocol(s) to your IND 132744 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) 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 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.

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.*[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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

REPORTING REQUIREMENTS

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

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval 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.

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[7].

If you have any questions, call 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
Acting Deputy Director
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Immediate Container Labeling

[7] https://www.uspnf.com/

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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