NDA 218230

NDA APPROVAL

GlaxoSmithKline, LLC
Attention: Xuying Wang, PhD
Associate Director, Global Regulatory Affairs
1250 South Collegeville Road
Mailstop UP 4400
Collegeville, PA 19426

Dear Dr. Wang:

Please refer to your new drug application (NDA) dated and received July 26, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Blujepa (gepotidacin) tablets.

This NDA provides for the use of Blujepa (gepotidacin) tablets for the treatment of female adult and pediatric patients 12 years of age and older weighing at least 40 kilograms (kg) with uncomplicated urinary tract infections (uUTI) caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus*, and *Enterococcus faecalis*.

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 the 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]

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

Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) 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.

CONTAINER LABELING

Submit final printed container labeling that is identical to the enclosed container labeling submitted on March 19, 2025, as soon it is available, but no more than 30 days after printing. Please submit this 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 Container Labeling for approved NDA 218230**." 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 Blujepa (gepotidacin) tablets shall be 24 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F). [See USP Controlled Room Temperature].

ADVISORY COMMITTEE

Your application for Blujepa was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the drug in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

SENTINEL/ARIA NOTIFICATION

The Food and Drug Administration Amendments Act of 2007 (FDAAA) required FDA to establish a national electronic system to monitor the safety of FDA-regulated medical products. In fulfillment of this mandate, FDA established the Sentinel System, which enables FDA to proactively monitor drug safety using electronic health data from multiple data sources that contribute to the Sentinel Distributed Database.

FDA plans to evaluate Blujepa in the Sentinel System as required for the implementation of section 505(o) of the FDCA.

[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.

We have determined that Sentinel's Active Postmarket Risk Identification and Analysis System, established under section 505(k)(3) of the FDCA, is insufficient to assess signals of serious risk of adverse maternal, fetal, and infant outcomes resulting from the use of gepotidacin during pregnancy.

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 studies requirement for ages birth to less than 2 years because necessary studies are impossible or highly impracticable as most urinary tract infections in this age group are considered complicated.

We are deferring submission of your pediatric studies for ages 2 years to less than 12 years for this application because this product is ready for approval for use in adults and pediatric patients 12 years and older and the studies in pediatric patients ages 2 years to less than 12 years have not been completed.

Your deferred pediatric studies required by section 505B(a) of the 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 FDCA. These required studies are listed below.

4822-1 Conduct an open-label, add-on, non-comparator study to evaluate the pharmacokinetics and safety of a single dose of oral gepotidacin administered in addition to antibacterial standard of care, in pediatric patients aged 2 years to less than 12 years with suspected or confirmed bacterial infection or who are receiving antibacterial prophylaxis.

Draft Protocol Submission:	05/2025
Final Protocol Submission:	10/2025
Study Completion:	12/2027
Final Report Submission:	06/2028

4822-2 Conduct an open-label, active-controlled comparator study to evaluate the safety and tolerability of oral gepotidacin in pediatric patients aged 2 years to less than 12 years with a confirmed or suspected uncomplicated UTI.

Draft Protocol Submission:	03/2027
Final Protocol Submission:	08/2027

Study Completion:	09/2032
Final Report Submission:	03/2033

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.[3]

Submit the protocols to your IND 111885, 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 identify an unexpected serious risk of the potential presence of gepotidacin in human breast milk resulting in effects on the breastfed infant, to assess signals of a serious risk of adverse maternal, fetal, and infant outcomes resulting from the use of gepotidacin during pregnancy, and to assess a signal of a serious risk of the development of drug resistance to gepotidacin.

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:

4822-3 Collect data from a prospective pregnancy exposure registry, preferably a disease-based multiproduct pregnancy registry, using a registry-based cohort study design that compares the maternal, fetal, and infant outcomes of women exposed to gepotidacin during pregnancy with comparator population(s) unexposed to gepotidacin. Align the study protocol with protocol(s) outside the U.S. to reach a target sample size.

[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.

The timetable you submitted on March 7, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2025
Final Protocol Submission:	04/2026
Interim Report Submission:	04/2029
Study Completion:	04/2032
Final Report Submission:	10/2032

The registry will identify and record pregnancy complications, major and minor congenital malformations, spontaneous abortion, stillbirths, pregnancy terminations, preterm births, small-for-gestational-age births, and any other adverse outcomes, including postnatal growth and development. These outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

4822-4 Conduct a retrospective pregnancy cohort study using claims or electronic health record data with medical chart validation that is adequately powered to assess small-for-gestational-age births, spontaneous abortions, major congenital malformations, stillbirths, and preterm births in individuals exposed to gepotidacin during pregnancy compared to appropriate comparator population(s).

The timetable you submitted on March 7, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2025
Final Protocol Submission:	04/2026
Interim Report Submission:	04/2028
Interim Report Submission:	04/2029
Interim Report Submission:	04/2030
Study Completion:	04/2032
Final Report Submission:	10/2032

4822-5 Perform a clinical lactation study (milk only or mother-infant pair study) in lactating women who have received gepotidacin to measure concentrations of gepotidacin in breast milk using a validated assay. Assess the effects on the breastfed infant, if available, based on the study population.

The timetable you submitted on March 7, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2025
Final Protocol Submission:	04/2026

Study Completion:	04/2028
Final Report Submission:	10/2028

4822-6 Conduct a United States surveillance study, or studies as appropriate, for 5 years from the date of marketing to determine if resistance to gepotidacin has developed in those organisms specific to the indication in the label.

The timetable you submitted on March 7, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	05/2025
Final Protocol Submission:	09/2025
Interim Report Submission:	09/2026
Interim Report Submission:	09/2027
Interim Report Submission:	09/2028
Interim Report Submission:	09/2029
Interim Report Submission:	09/2030
Study Completion:	06/2031
Final Report Submission:	09/2031

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 protocols to your IND 111885 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

[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.

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.*[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).

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.

[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

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].

If you have any questions, contact J. Christopher Davi, MS, Senior Regulatory Project Manager, at (301) 796-0702 or christopher.davi@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Adam Sherwat, MD
Deputy Office Director
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Container Labeling

[8] 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/

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