

NDA 212271

**NDA APPROVAL**

Meitheal Pharmaceuticals Inc.  
Attention: Roopang Shah  
Director, Regulatory Affairs  
8700 West Bryn Mawr, Suite 600S  
Chicago, IL 60631

Dear Roopang Shah:

Please refer to your new drug application (NDA) received on October 31, 2018, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Contepo (fosfomycin) for injection.

We acknowledge receipt of your amendment dated April 29, 2025, which constituted a complete response to our December 11, 2024, action letter.

This NDA provides for the use of Contepo (fosfomycin) for injection for the treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI), including acute pyelonephritis, caused by susceptible isolates of *Escherichia coli* and *Klebsiella pneumoniae*.

### **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.<sup>1</sup> 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*.<sup>2</sup>

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 212271.**” 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 Contepo (fosfomycin) for injection shall be 36 months from the date of manufacture when stored at 20 °C to 25 °C (68 °F to 77 °F); excursions permitted between 15 °C to 30 °C (59 °F to 86 °F).

### **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 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.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

4908-1 Conduct an open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability of Contepo in children from birth (full term) to less than 12 years of age with suspected or confirmed gram-negative bacterial infection, or for peri-operative prophylaxis, and receiving other systemic antibiotic standard of care therapy.

Final Protocol Submission:	Submitted
Study Completion:	02/2027
Final Report Submission:	04/2027

4908-2 Conduct an open-label, single arm study to evaluate the pharmacokinetics and safety of Contepo in children from birth (full term 37 weeks) to less than 18 years of age with complicated urinary tract infections (cUTI).

Draft Protocol Submission:	03/2027
Final Protocol Submission:	07/2027
Study Completion:	03/2030
Final Report Submission:	09/2030

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.<sup>3</sup>

Submit the protocols to your IND 118777, 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 fosfomycin in human breast milk

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<sup>3</sup> 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>.

resulting in effects on the breastfed infant or to assess a signal of serious risk of the development of drug resistance to fosfomycin.

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

4908-3 Conduct a clinical lactation study (milk-only) in lactating women administered Contepo to determine the concentrations of fosfomycin and its major metabolites in human milk using validated bioanalytical methods.

Draft Protocol Submission:	05/2026
Final Protocol Submission:	11/2026
Study Completion:	11/2028
Final Report Submission:	05/2029

4908-4 Conduct a U.S. surveillance study over a five-year period after the introduction of Contepo (fosfomycin) for injection to the market to determine if resistance or decreased susceptibility to fosfomycin is occurring in the target population of bacteria that are in the approved Contepo label.

Final Protocol Submission:	04/2026
First Interim Study Report Submission:	05/2027
Second Interim Study Report Submission:	05/2028
Third Interim Study Report Submission:	05/2029
Fourth Interim Study Report Submission:	05/2030
Fifth Interim Study Report Submission:	05/2031
Study Completion:	08/2031
Final Report Submission:	11/2031

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.<sup>4</sup>

Submit clinical protocols to your IND 118777 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).**

<sup>4</sup> 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>.

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*.<sup>5</sup>

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.<sup>6</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>7</sup>

## **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

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<sup>5</sup> For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/media/128163/download>.

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>7</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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<sup>8</sup>.

If you have any questions, contact Hany Meskelu, PharmD, Regulatory Project Manager, at 240-402-0183 or [Hany.Meskelu@fda.hhs.gov](mailto:Hany.Meskelu@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

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<sup>8</sup> <https://www.uspnf.com/>

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**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.**  
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/s/  
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