NDA 214520

LPAD PATHWAY APPROVAL

CorMedix Inc.
Attention: Phoebe Mounts, PhD, Esq.
Executive Vice President and General Counsel
5825 Bellanca Drive
Elkridge, MD 21075

Dear Dr. Mounts:

Please refer to your new drug application (NDA) dated and received June 30, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Defencath (taurolidine and heparin) catheter lock solution.

We also refer to your written request dated May 15, 2023, for approval under section 506(h) of the FDCA for the Limited Population Pathway for Antibacterial and Antifungal Drugs (the LPAD Pathway).

We acknowledge receipt of your amendment dated May 15, 2023, which constituted a complete response to our August 4, 2022, action letter.

This NDA provides for the use of Defencath (taurolidine and heparin) catheter lock solution to reduce the incidence of catheter-related bloodstream infections (CRBSI) in adult patients with kidney failure receiving chronic hemodialysis (HD) through a central venous catheter (CVC). This drug is indicated for use in a limited and specific population of patients.

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.

LPAD PATHWAY APPROVAL

This application is furthermore approved under section 506(h) of the FDCA and marketing of this drug product is subject to the requirements for labeling and promotional materials described therein.

Under section 506(h)(7), FDA may terminate the limitations associated with the LPAD pathway when FDA has determined that the product is safe and effective for a broader population. The additional data supporting approval for the broader population should

demonstrate the conditions of the LPAD pathway are no longer necessary for the drug product. If you decide to conduct clinical trials to support termination of limitations, submit final reports to this NDA as a supplemental application. For administrative purposes, designate this submission "**LPAD Pathway Termination Request**."

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 214520**." 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 Defencath (taurolidine and heparin) catheter lock solution shall be 36 months from the date of manufacture when stored at controlled room temperature of 20°C to 25°C (68°F to 77°F); excursions are permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

ADVISORY COMMITTEE

Your application for Defencath was not referred to an FDA advisory committee because outside expertise was not necessary.

[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.

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 study because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required under 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.

4028-1 An open-label, two-arm (Defencath vs. standard of care) study to assess safety and time to CRBSI in subjects from birth to less than 18 years of age with kidney failure receiving hemodialysis via a central venous catheter.

Final Protocol Submission:	02/2024
Study Completion:	12/2027
Final Report Submission:	06/2028

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 to your IND 113764, 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.

PROMOTIONAL MATERIALS

Under section 506(h) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 356(h)), you are required to submit copies of all promotional materials, including promotional labeling and advertisements, related to the drug subject to this marketing approval at

[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.

least 30 calendar days prior to dissemination of the materials. You should submit your materials with a cover letter that clearly identifies the submission as a "Pre-Submission of Promotional Materials for a Limited Population Pathway Antibacterial or Antifungal Drug." If you have questions, you may contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200 and ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue. Please note that you are required to continue to comply with Agency regulation and submit all specimens of mailing pieces and any other labeling or advertising devised for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement (21 CFR 314.81(b)(3)(i) and 21 CFR 601.12(f)(4)).

You may also seek advisory comment from the Agency on your promotional materials. Should you voluntarily choose to seek advisory comment, we ask that your submission include a separate, detailed cover letter that indicates you are seeking advisory comment together with three copies each of the promotional materials, annotated references, and approved package insert (PI), Medication Guide, and patient PI (as applicable).

Send each submission directly to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotions (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit promotional materials and any requests for advisory comment electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.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[4].

If you have any questions, call Kristine Park, PhD, RAC, PMP, Senior Regulatory Health Project Manager, at (301) 796-0471.

Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Director
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

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

[4] 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/

JOHN J FARLEY
11/15/2023 06:28:26 AM