NDA 212862/S-008

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Mylan Ireland Limited, a Viatris Company
c/o Mylan Pharmaceuticals Inc., a Viatris Company
Attention: Robert Barto
Senior Director, Regulatory Affairs
3711 Collins Ferry Road
Morgantown, WV 26505

Dear Robert Barto:

Please refer to your supplemental new drug application (sNDA) dated January 23, 2024, received January 23, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for pretomanid tablets, 200 mg.

This Prior Approval supplemental new drug application provides for the following changes:

1) Modification of the dosage regimen (now referred to as "Preferred" and "Alternative" dosage regimens) for the linezolid component in the bedaquiline, pretomanid, linezolid (BPaL) combination regimen based on safety and efficacy information from the ZeNix Trial (PMR 3682-6/NCT03086486).
2) Addition of an alternative dosage regimen for the bedaquiline component of the BPaL combination regimen based on safety and efficacy information from the ZeNix Trial (PMR 3682-6/NCT03086486).
3) Inclusion of information on the administration of a crushed pretomanid tablet based on in vitro studies.

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

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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 Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, 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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 212862/S-008**." Approval of this submission by FDA is not required before the labeling is used.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labeling must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of*

[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.

Proprietary Names and *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027*.)

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.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

3682-6 Conduct the ZeNix trial to evaluate various doses and treatment durations of linezolid plus bedaquiline and Pretomanid Tablets for treatment of extensively drug-resistant pulmonary tuberculosis.

We have reviewed your July 31, 2023, submission and conclude that the above requirement was fulfilled.

We remind you that there are postmarketing requirements listed in the August 14, 2019, approval letter that are still open.

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 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).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

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

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- 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
11/22/2024 12:48:26 PM