NDA 209939/S-015
NDA 209940/S-015
NDA 219104/S-001

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Merck Sharp and Dohme LLC., a subsidiary of Merck & Co., Inc.
Attention: Megan Wise, PhD
Senior Director, Global Regulatory Affairs
351 N. Sumneytown Pike, UG2D-068
North Wales, PA 19454

Dear Dr. Wise:

Please refer to your supplemental new drug applications (sNDAs) dated and received August 7, 2024 (NDAs 209939 and 209940) and September 13, 2024 (NDA 219104), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prevymis (letermovir) tablets, 240 mg and 480 mg (NDA 209939), Prevymis (letermovir) injection, 240 mg/12 ml and 480 mg/24 ml (NDA 209940), and Prevymis (letermovir) oral pellets, 20 mg or 120 mg per packet (NDA 219104).

These Prior Approval sNDAs provide for the following change to the labeling:

- To update CLINICAL PHARMACOLOGY, Microbiology subsection with the additional phenotypic analysis data for letermovir against HCMV with the pUL56 (S229Y or M329I) and to remove information regarding pUL89 (D344Y) substitutions from the Prescribing Information

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are 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, Patient Package Insert, and Instructions for Use), 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 application(s) that include labeling changes for these NDAs, 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 these supplemental applications, 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).

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 none of these criteria apply to your applications, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

[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.

We have received your submissions dated June 27, 2024, containing the final report for the following postmarketing requirement listed in the June 5, 2023 approval letter.

4457-1 Conduct phenotypic analysis of letermovir against human CMV (HCMV) mutants carrying the following pUL56 and pUL89 substitutions:

- pUL56: S229Y, M329I
- pUL89: D344Y

Include previously identified substitutions with a range of susceptibilities from low fold change (e.g., pUL56: L257I or S229F) to high fold change (e.g., pUL56: C325Y) as references.

We have reviewed your submissions and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements acknowledged in our June 5, 2023 approval letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 314.81(b)(2)(vii).

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 Saebyeol Jang, Senior Regulatory Project Manager at 240-402-9953 or saebyeol.jang@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Wendy Carter, DO
Director
Division of Antivirals
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert (Version approved August 30, 2024)
  - Instructions for Use (Version approved August 30, 2024)

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/

POONAM MISHRA
01/30/2025 10:18:41 AM
on behalf of the Division Director