



NDA 209939/S-05
NDA 209940/S-03

SUPPLEMENT APPROVAL

Merck Sharp and Dohme Corp.,
a Subsidiary of Merck and Co., Inc.
Attention: Laurie J. MacDonald, MD
Associate Vice President, Global Regulatory Affairs
351 N. Sumneytown Pike
P.O. Box 1000, UG2D-68
North Wales, PA 19454-2505

Dear Dr. MacDonald:

Please refer to your supplemental new drug applications (sNDAs) dated and received March 4, 2019 (NDA 209939), March 7, 2019 (NDA 209940), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for PREVMIS (letermovir) tablets, 240 mg and 480 mg, and PREVMIS (letermovir) injection, 240 mg/12 ml and 480 mg/24 ml in single-dose vials.

These Prior Approval supplemental new drug applications provide for the following:

- To update DRUG INTERACTIONS section with information that PREVMIS is a substrate of P-gp transporters and UGT1A1/3 enzymes and co-administration of PREVMIS with inducers of transporters (e.g. P-gp) and/or enzymes (e.g. UGTs) is not recommended due to the potential for decrease in letermovir plasma concentrations.
- To revise the clinical comment pertaining to rifampin in the DRUG INTERACTIONS section from "Co-administration of PREVMIS with rifampin is not recommended" to "Co-administration of PREVMIS with rifampin is not recommended due to potential for loss of efficacy of PREVMIS".
- To add several UGT and/or P-gp inducers to Table 3 in DRUG INTERACTIONS section and incorporate a clinical comment similar to that for rifampin because these inducers may also result in a clinically relevant decrease in letermovir exposures.
- To update CLINICAL PHARMACOLOGY, Pharmacokinetics Table 5 with pharmacokinetic data from the drug-drug interaction trial of PREVMIS with rifampin.

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.

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 Patient Package Insert), 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).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and*

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>.

*Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

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, call Christine Kim, PharmD, Regulatory Project Manager, at (301) 796-5964 or at the mainline at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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
08/29/2019 08:06:00 AM
on behalf of Debra Birnkrant