DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205786/S-006
NDA 022145/S-037
NDA 203045/S-014

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Merck Sharp & Dohme Corp.
Attention: Chitrananda Abeygunawardana, Ph.D.
Director, Regulatory Liaison, Global Regulatory Affairs
351 North Sumneytown Pike
P.O. Box 1000, UG2D-68
North Wales, PA 19454

Dear Dr. Abeygunawardana:

Please refer to your Supplemental New Drug Application (sNDA) dated and received on May 25, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ISENTRESS® (raltegravir) oral suspension, 100 mg (NDA 205786).

This Prior Approval supplemental new drug application proposes to update the content of labeling with data from pediatric study IMPAACT P1110/Merck P080 in HIV exposed neonates ages 0-4 weeks and weighing at least 2 kg and to update the Instructions for Use to include new syringe sizes and mixing instructions.

In addition, this supplement provides a response to the Written Request dated August 18, 2006.

We also refer to your sNDAs dated and received June 9, 2017 for ISENTRESS® (raltegravir) film-coated tablets, 400 mg and ISENTRESS HD® (raltegravir) film-coated tablets, 600 mg (NDA 22145) and ISENTRESS® (raltegravir) chewable tablets, 100 mg scored and 25 mg (NDA 203045).

These Prior Approval supplemental new drug applications were provided to update the shared ISENTRESS® (raltegravir) labeling with the above pediatric data.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert, text for the 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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 IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 205786/S-006**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We reference the waiver for pediatric study requirements for ages 2-16 granted on December 20, 2013 (NDA 205786/S-006).

We note that you have fulfilled the pediatric studies requirement for neonates ages 0-4 weeks, and for all relevant pediatric age groups for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated May 25, 2017, containing the final report for the following postmarketing requirement listed in the December 20, 2013, approval letter:

1881-1 Deferred pediatric study under PREA to evaluate the safety and pharmacokinetics of raltegravir in HIV-exposed neonates (born to HIV-infected mothers). This multiple-dose pharmacokinetic and safety study will evaluate raltegravir in addition to the standard of care in HIV-exposed neonates from ages 0 to 4-6 weeks. HIV-exposed neonates will have safety assessments, on or off treatment (as appropriate), for a minimum of 24 weeks after start of raltegravir therapy.

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

This completes your postmarketing requirement acknowledged in our December 20, 2013, letter.

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 package insert(s) 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 (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must submit final promotional materials and package insert(s), 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 http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or 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).

If you have any questions, call Christian Yoder, Regulatory Project Manager, at (240) 402-9990 or (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
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JEFFREY S MURRAY
11/22/2017