DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205786
NDA 22145 S-031
NDA 203045 S-009

NDA APPROVAL
SUPPLEMENT APPROVAL

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

Dear Dr. Abeygunawardana:

Please refer to your New Drug Application (NDA) dated June 26, 2013, received June 27, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ISENTRESS® (raltegravir) for oral suspension, 100 mg.

Please also refer to your Supplemental New Drug Applications (sNDAs) dated June 25, 2013, received June 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ISENTRESS® (raltegravir) film-coated tablets, 400 mg, and ISENTRESS® (raltegravir) chewable tablets, 25 mg and 100 mg.

We acknowledge receipt of your amendments dated:

July 11, 2013	September 24, 2013	November 20, 2013
July 18, 2013	October 1, 2013	November 21, 2013
July 31, 2013	October 9, 2013	December 2, 2013
August 16, 2013	October 14, 2013	December 10, 2013
August 19, 2013	October 21, 2013	December 13, 2013
August 28, 2013	October 31, 2013	December 18, 2013
September 6, 2013	November 5, 2013	December 19, 2013
September 18, 2013	November 7, 2013	

This new drug application provides for the use of a new dosage form, ISENTRESS® (raltegravir) for oral suspension, in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients 4 weeks of age and older, weighing at least 3 kg to less than 20 kg.

These Prior Approval supplemental new drug applications update the shared ISENTRESS® (raltegravir) labeling with information on use of the new dosage form, ISENTRESS® (raltegravir) for oral suspension.

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 text.

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 and text for the patient package insert). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

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 *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**Final Printed Carton and Container Labels for approved NDA 205786**" and **Final Printed Carton and Container Labels for approved NDA 203045/S-009."** Approval of these submissions by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Katherine Schumann, M.S.
Food and Drug Administration

Center for Drug Evaluation and Research
White Oak Building 22, Room: 6360
10903 New Hampshire Avenue
Silver Spring, Maryland
Use zip code **20903** *if shipping via United States Postal Service (USPS).*
Use zip code **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

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 are waiving the pediatric study requirement for ISENTRESS® (raltegravir) for oral suspension (NDA 205786) for ages 2 to 16 years because the product does not represent a meaningful therapeutic benefit over existing therapies (film-coated tablets and chewable tablets) for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

We are deferring submission of your pediatric study for ages 0 to 4 weeks for this application because this product is ready for approval for use in pediatric subjects older than 4 weeks and pediatric studies in the remaining pediatric populations have not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act 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)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

We reference the deferral granted under NDA 203045 in the March 16, 2012, new postmarketing requirement 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.

Final Protocol Submission: December 2012
Study Completion: April 2014
Final Report Submission: January 2015

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDAs with the proposed labeling changes you believe are warranted based on the data derived from these studies. 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.

We note that you have fulfilled the pediatric study requirement for ages 4 weeks to less than 2 years.

582-3 Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric subjects from 4 weeks to 2 years of age. This study will determine raltegravir exposure (pharmacokinetic profile) followed by 24 weeks of dosing. Efficacy will be based on viral load reduction through 24 weeks of dosing and safety will be monitored for a minimum of 24 weeks to support raltegravir dose selection, safety, and efficacy in this population.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. 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.

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 Katherine Schumann, M.S., Regulatory Project Manager, at (301) 796-1182 or the Division's main number at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
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
12/20/2013