DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205786 S-3
NDA 203045 S-12
NDA 22145 S-35

SUPPLEMENT APPROVAL

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 Applications (sNDA) dated August 20, 2014, received August 20, 2014 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ISENTRESS® (raltegravir) for oral suspension, ISENTRESS® (raltegravir) chewable tablets, for oral use, and ISENTRESS® (raltegravir) film-coated tablets, for oral use.

We acknowledge receipt of your amendments dated December 18, 2014, February 10, 2015 and February 16, 2015.

These prior approval supplemental new drug applications propose the following changes:

- To update the DRUG INTERACTION section of the labeling with subsection, 7.3 Drugs without Clinically Significant Interactions with Isentress. Drugs that met this criteria were removed from Table 8 and placed in this section.

- To update CLINICAL PHARMACOLOGY, Table 10, with information regarding aluminum and magnesium hydroxide antacids.

- To update CLINICAL PHARMACOLOGY, Microbiology- Resistance subsection with information the 240 week results from the STARMRK trial.

- To update CLINICAL PHARMACOLOGY, Microbiology with a Cross Resistance subsection that provides information related to the integrase strand transfer inhibitors, elvitegravir and dolutegravir.

- To remove telaprevir information from the labeling.

- To update the Patient Information section entitled, "What should I tell my doctor before taking ISENTRESS? subtitle Pregnancy Registry to remove information about Isentress in breast milk.

- To reformat the information in the Patient Information section entitled, "Tell your doctor about all the medicines you take".

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 and text for the patient package), 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 includes 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 MS Word format, that includes the changes approved in these supplemental applications, 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).

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 Mammah Sia Borbor, M.S., M.B.A., Regulatory Project Manager, at (301) 796-7731 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

ENCLOSURE(S):
Content of Labeling

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

/s/

POONAM MISHRA
02/20/2015