DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205395

NDA APPROVAL

Janssen Products, LP
Attention: Karen Gerry, BSc
Manager, Global Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560

Dear Ms. Gerry:

Please refer to your New Drug Application (NDA) dated March 31, 2014 and received March 31, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Prezcobix™ (darunavir and cobicistat) tablet, 800 mg/150 mg for oral use.

We also refer to our approval letter dated January 29, 2015 which contained the following errors:

1. The Table numbers in the Prescribing Information were incorrect.

This replacement approval letter incorporates the correction of the errors. The effective approval date will remain January 29, 2015 the date of the original approval letter.

We acknowledge receipt of your amendments dated:

April 11, 2014	August 4, 2014	November 26, 2014
April 23, 2014	August 8, 2014	December 16, 2014
May 6, 2014	August 11, 2014	December 18, 2014
June 2, 2014	August 13, 2014	December 22, 2014
June 24, 2014	September 12, 2014	January 7, 2015
June 27, 2014	October 1, 2014	January 12, 2015
June 30, 2014	October 15, 2014	January 14, 2015
July 8, 2014	October 17, 2014	January 21, 2015
July 14, 2014	November 24, 2014	January 26, 2015
August 4, 2014	November 25, 2014	January 28, 2015

This new drug application provides for the use of Prezcobix™ (darunavir and cobicistat) in combination with other antiretroviral agents for treatment of HIV-1 infection.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is 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, text for the patient information). 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.

IMMEDIATE CONTAINER LABEL

Submit the final printed immediate container label that is identical to the enclosed immediate container label, as soon as it is available, but no more than 30 days after it is printed. Please submit the label 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 this submission "**Final Printed Container Label for approved NDA 205395**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product 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:

Nina Mani
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6317
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 ages, birth to less than 3 years of age because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group. Use of darunavir, a component of the fixed dose combination (FDC) product, is not appropriate in pediatric patients < 3 years of age. This decision is based on the results of juvenile rat toxicology studies that provide evidence of potential safety risk as a result of accumulation of drug in the brain.

We are also waiving the pediatric studies requirement for children ages 3 years to less than 18 years weighing less than 15 kilograms (kg) because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age and weight group. In addition, multiple FDC formulations would be required to be developed to accommodate the various weight bands in the small number of pediatric patients below 15 kg.

We are deferring submission of your pediatric studies for children ages 3 years to less than 18 years of age and who weigh 15 kg or more for this application because the product is ready for approval in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. These required studies are listed below.

2845-1 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 3 years to less than 6 years of age and weighing at least 15 kg. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC age-appropriate formulation in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children ages 3 years to less than 6 years may not be required if the dosing recommendation for the FDC age-appropriate formulation can be supported by pediatric trials already conducted with the individual drug products and if the age-appropriate FDC produces similar exposures as the individual components.

Final Protocol Submission:	03/31/2020
Study Completion:	12/31/2020
Final Report Submission:	12/31/2021

2845-2 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 6 years to less than 12 years of age and weighing at least 15 kg. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC age-appropriate formulation in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children ages 6 years to less than 12 years may not be required if the dosing recommendation for the FDC age-appropriate formulation can be supported by pediatric trials already conducted with the individual drug products and if the age-appropriate FDC produces similar exposures as the individual components.

Final Protocol Submission:	03/31/2020
Study Completion:	12/31/2020
Final Report Submission:	12/31/2021

2845-3 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed-dose combination (FDC) tablets in HIV-infected pediatric subjects 12 years to less than 18 years of age. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC tablets in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children 12 years to less than 18 years of age may not be required if the dosing recommendation for the FDC tablets can be supported by pediatric trials already conducted with the individual drug products and if the FDC produces similar exposures as the individual components.

Final Protocol Submission:	03/31/2020
Study Completion:	12/31/2020
Final Report Submission:	12/31/2021

Submit the protocols to your IND 113198, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA 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.

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. 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.

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 Nina Mani, Regulatory Project Manager, at (240) 402-0333.

Sincerely,

{See appended electronic signature page}

Jeffrey S. Murray, MD, MPH
Deputy Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
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
01/29/2015