

NDA 021976/S-56

NDA 202895/S-27

SUPPLEMENT APPROVAL

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

Dear Ms. Gerry:

Please refer to your supplemental new drug applications (sNDAs) dated and received November 30, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for PREZISTA[®] (darunavir) 75 mg, 150 mg, 600 mg and 800 mg tablets (NDA 021976) and PREZISTA[®] (darunavir) 100 mg/mL, oral solution (NDA 202895).

These Prior Approval supplemental new drug applications provide for revisions to the following sections of the Prescribing Information:

- **CONTRAINDICATIONS:**
 - Ranolazine and dronedarone were removed from their respective drug categories (“Antianginal” and “Antiarrhythmic”) and placed with the addition of ivabradine under the new category of “Cardiac Disorders”
 - Naloxegol was added under the new category of “Opioid Antagonist”
- **WARNINGS AND PRECAUTIONS:**
 - Update to Section 5.8 “Immune Reconstitution Syndrome”, with the addition of autoimmune hepatitis
- **DRUG INTERACTIONS, Table 10, was updated:**
 - Antifungals: information on use of isavuconazole
 - Antimycobacterials: removal of cobicistat
 - Cardiac Disorders: new category added with drugs previously listed under “Other Agents, Antiarrhythmics and Antianginal” moved to this category. Added information on use of ivabradine
 - Systemic/Inhaled/ Nasal/Ophthalmic Corticosteroids: addition of prednisone as a corticosteroid less affected by strong CYP3A inhibitor relative to other corticosteroids
 - Herbal product: removal of cobicistat
 - Hormonal Contraceptives: recategorization of heading, previously read “Oral contraceptives/estrogen”
 - Immunosuppressant/neoplastic: information on use of irinotecan

- Opioid Antagonist: information on use of naloxegol
- Urinary Antispasmodics: information on use of fesoterodine and solifenacin
- Ivabradine and naloxegol were added to the Patient Package Insert under the heading “Who should not take PREZISTA?, Do not take PREZISTA with any medicine that contains:”.

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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

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 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).

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>.

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 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, contact Philip Villasurda, Regulatory Project Manager, at Philip.Villasurda@fda.hhs.gov or call at (301) 796-2586 or (301) 796-1500.

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>

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

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

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
05/28/2019 04:09:54 PM
on behalf of Debra Birnkrant