NDA 202379/S-027 and S-028

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING COMMITMENT

Janssen Biotech, Inc.
Attention: Tamara Mazza, PhD
Associate Director, Global Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560

Dear Dr. Mazza:

Please refer to your supplemental new drug applications (sNDAs) dated January 4, 2019 (S-027), and January 29, 2019 (S-028), received January 4, 2019, and January 29, 2019, respectively, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zytiga® (abiraterone acetate) Tablets, 250 mg and 500 mg.

Prior Approval supplemental new drug application S-027 provides for updates to the Full Prescribing Information to include risk of QT prolongation and Torsades de Pointes observed in patients experiencing hypokalemia in association with Zytiga treatment. Additionally, this supplement provides for revisions to the Full Prescribing Information to state that radium 223 dichloride is not recommended for use in combination with abiraterone acetate and prednisone outside of clinical trials based on results from Phase 3 study ERA-223.

Prior Approval supplemental new drug application S-028 provides for updates to the Full Prescribing Information based on the final analysis for overall survival in clinical trial, 212082PCR3011, entitled, “A Randomized, Double-blind, Comparative Study of Abiraterone Acetate Plus Low Dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Subjects With High Risk, Metastatic Hormone-Naive Prostate Cancer.” This submission includes the final report to postmarketing commitment (PMC) 3330-1 from the February 7, 2018, approval letter.

In addition, these Prior Approval supplemental new drug applications provide for revisions to the Contraindications, Embryo-Fetal Toxicity, Pregnancy, and Lactation Sections. These revisions are more consistent with the current FDA Pregnancy and Lactation Labeling Rule (PLLR) and Guidance and the FDA Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials Guidance. It also provides for revisions to the Pharmacodynamic Section to be consistent with the current labeling guidance for the Clinical Pharmacology Section. Furthermore, these supplements revised one of the warning and precautions to read as “Hypokalemia, Fluid Retention, and Cardiovascular Adverse Reactions due to Mineralocorticoid Excess.”

APPROVAL & LABELING

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

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 (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).

REQUIRED PEDIATRIC ASSESSMENTS

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

Because none of these criteria apply to your applications, you are exempt from this requirement.

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[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.

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submission dated January 29, 2019, containing the final report for the following postmarketing commitment listed in the February 7, 2018, approval letter.

3330-1 Submit the final analysis for overall survival, datasets, and labeling with the final report for the ongoing clinical trial, 212082PCR3011, entitled, "A Randomized, Double-blind, Comparative Study of Abiraterone Acetate Plus Low Dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Subjects With High Risk, Metastatic Hormone-Naive Prostate Cancer."

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

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our February 7, 2018, 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 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

[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.

[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, call Sherry Hou, PharmD, Regulatory Project Manager, at (240) 402-1813.

Sincerely,

{See appended electronic signature page}

Amna Ibrahim, MD
Deputy Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[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

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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/

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