NDA 212018/S-007
NDA 212018/S-008
NDA 212018/S-009

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENTS/COMMITMENTS

Janssen Biotech, Inc.
Attention: Bawa Rabindran, MS
Associate Director, Global Regulatory Affairs
920 U.S. Highway 202, P.O. Box 300
Raritan, NJ 08869

Dear Bawa Rabindran:

Please refer to your supplemental new drug applications (sNDA) dated July 21, 2023, received July 21, 2023 (S-007), and dated August 28, 2023, received August 28, 2023 (S-008), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Balversa (erdafitinib).

For administrative purposes, we separated the efficacy supplement (S-008) that you submitted into two efficacy supplements. Please see information on the two supplements below:

- NDA 212018/S-008: SE-7 Accelerated Approval Confirmatory Study (Subpart H)
- NDA 212018/S-009: SE-1 New Indication or significant modification to existing indication

Supplement 007 provides for:

1. Updated information on the effect of erdafitinib on the pharmacokinetics (PK) of midazolam and metformin, as well as potential drug-drug interaction (DDI) with CYP2C9 inducers or strong CYP3A4 inducers based on data from the 42756493NAP1001 Study (CSR submitted on January 19, 2023, to NDA 212018 (SN0235) to fulfill PMC 3561-4) and 42756493BLC2001 DDI sub-study (CSR submitted on March 28, 2023 to NDA 212018 (SN0249) to fulfill PMR 3561-3 and PMC 3561-5).
2. Addition of hyponatremia and blood creatinine increased as adverse reactions.

Supplement 008 provides for analysis and datasets with the final report of the Subpart H Postmarketing Requirement 3561-1 as described in the NDA approval letter dated April 12, 2019:

PMR 3561-1: Submit the analysis, and datasets with the final report demonstrating clinical benefit of erdafitinib in patients with locally advanced and metastatic urothelial carcinoma with susceptible FGFR 3 or FGFR 2 genetic alterations from clinical trial BLC3001 entitled; "*A Phase 3 Study of Erdafitinib Compared with Vinflunine or Docetaxel or Pembrolizumab in Subjects with Advanced Urothelial Cancer and Selected FGFR Gene Aberrations*."

Supplement 009 provides for regular approval for the following modification to the existing indication: Balversa for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible *FGFR3* genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy.

APPROVAL & LABELING

We have completed our review of this application. It is 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, 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 the 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.

SUBPART H FULFILLED

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 314.510.

FULFILLMENT OF POSTMARKETING REQUIREMENTS/COMMITMENTS

We have received your submissions dated January 19, 2023, March 28, 2023, and August 28, 2023, containing the final reports for the following postmarketing requirements and commitments listed in the April 12, 2019, approval letter.

3561-1 Submit the analysis, and datasets with the final report demonstrating clinical benefit of erdafitinib in patients with locally advanced and metastatic urothelial carcinoma with susceptible FGFR 3 or FGFR 2 genetic alterations from clinical trial BLC3001 entitled; “A Phase 3 Study of Erdafitinib Compared with Vinflunine or Docetaxel or Pembrolizumab in Subjects with Advanced Urothelial Cancer and Selected FGFR Gene Aberrations.”

3561-3 Conduct a clinical pharmacokinetic trial that evaluates the effect of repeated doses of erdafitinib on the single dose pharmacokinetics of a sensitive CYP3A substrate (e.g., midazolam), to address the potential for excessive drug toxicity or decreased drug exposure, and to determine appropriate dosing recommendations when coadministering erdafitinib with a sensitive CYP3A substrate. This trial should be designed and conducted in accordance with the FDA Draft Guidance for Industry: Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications. Submit the analysis and datasets with the final report.

3561-4 Conduct a clinical pharmacokinetic trial that evaluates the effect of repeated doses of a strong inducer (e.g., rifampin) of CYP2C9 and CYP3A on the single dose pharmacokinetics of erdafitinib to assess the magnitude of decreased drug exposure and to determine appropriate dosing recommendations when erdafitinib is coadministered with CYP2C9 and CYP3A inducers. This trial should be designed and conducted in accordance with the FDA Draft Guidance for Industry: Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications. Submit the analysis and datasets with the final report.

3561-5 Conduct a clinical pharmacokinetic study that evaluates the effect of repeated doses of erdafitinib (at steady-state) on the single dose pharmacokinetics of a probe substrate of OCT2 to determine appropriate

dosing recommendations for OCT2 substrate when it is coadministered with erdafitinib. This study should be designed and conducted in accordance with the FDA Draft Guidance for Industry: Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications. Submit the analysis and datasets with the final report.

We have reviewed your submissions and conclude that the above requirements and commitments were fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our April 12, 2019, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMCs in your annual report required under 21 CFR 314.81(b)(2)(vii) of the FD&CA.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final 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]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to the FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to the FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

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 Dana Kappel, Regulatory Project Manager, at (301) 796-8768 or at Dana.Kappel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Daniel Suzman, MD
Deputy Director
Division of Oncology 1
Office of Oncologic Diseases
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/

DANIEL L SUZMAN
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