NDA 211810/S-3

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT/COMMITMENTS

Daiichi Sankyo, Inc
Attention: Yoshiyuki Hattori, Ph.D.
Associate Director, Regulatory Affairs Oncology
211 Mount Airy Road
Basking Ridge, NJ 07920-2311

Dear Dr. Hattori:

Please refer to your supplemental new drug application (sNDA) submitted and received October 25, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Turalio (pexidartinib) capsules, 200 mg.

This Prior Approval supplemental new drug application provides for revisions to Sections 2.4 Concomitant Use of Moderate or Strong CYP3A Inhibitors; 5.3 Embryo-Fetal Toxicity; 7.2 Effect of Other Drugs on TURALIO; 7.3 Effect of TURALIO on Other Drugs; 8.3 Females and Males of Reproductive Potential; and 12.3 Pharmacokinetics of the package insert (PI). Additional revisions were made to Section 17 and to the Medication Guide for consistency with changes to Sections 5.3, 7.3 and 8.3.

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.

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 Medication Guide), 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.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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 application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENTS

We have received your submission dated August 13, 2019, containing the final report for the following postmarketing requirement listed in the August 2, 2019, approval letter.

3673-4 Complete a pharmacokinetic trial to determine the effect of a moderate CYP3A4 inhibitor on the exposure to pexidartinib in accordance with the FDA Guidance for Industry entitled “Clinical Drug Interaction Studies-Study Design, Data Analysis, and Clinical Implications” found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292362.pdf.

[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.

We have received your submission dated September 27, 2019, containing the final reports for the following postmarketing commitments listed in the August 2, 2019, approval letter.

3673-5 Submit the final trial report and results from the ongoing DDI Study PL3397-AU126 evaluating the effect of pexidartinib on the exposure of midazolam (a CYP3A4 substrate) and tolbutamide (a CYP2C9 substrate).

3673-6 Complete a pharmacokinetic trial or PBPK modeling to determine the effect of a moderate CYP3A4 inducer on the exposure to pexidartinib following single and multiple doses of pexidartinib in accordance with the FDA Guidance for Industry entitled "Clinical Drug Interaction Studies – Study design, Data Analysis, and Clinical Implications" found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292362.pdf.

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

We remind you that there are postmarketing requirements and a postmarketing commitment listed in the August 2, 2019, approval letter that are still open.

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]

[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.

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]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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety 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) to the address above, by fax to 301-847-8444, or 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*.

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, you may contact Nataliya Fesenko, Pharm.D., Regulatory Health Project Manager, at (240) 402-6376.

Sincerely,

{See appended electronic signature page}

Abhilasha Nair, M.D.
Associate Director for Safety (Acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
    - Prescribing Information

[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

- Medication Guide

APPEARS THIS WAY ON ORIGINAL

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/

ABHILASHA NAIR
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