BLA 125514/S-157

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING COMMITMENT

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.
Attention: June Ancona
Associate Director, Global Regulatory Affairs
351 North Sumneytown Pike
P.O. Box 1000, UG2D68
North Wales, PA 19454-2505

Dear June Ancona:

Please refer to your supplemental biologics license application (sBLA), dated January 30, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab).

This Prior Approval supplemental biologics license application provides to update the label to include the updated efficacy results from the protocol-specified third interim analysis of study KEYNOTE-564 (KN-564).

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.

WAIVER OF HIGHLIGHTS 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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

[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 via publicly available labeling repositories.

Also, within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which the FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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(s) 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 COMMITMENT

We have received your submission dated January 30, 2024, reporting on the following postmarketing commitment listed in the November 17, 2021, approval letter for BLA 125514/S-113.

4166-1 Conduct clinical trial KEYNOTE-564, titled, "A Phase III, Randomized, Double-Blind, placebo-controlled clinical trial of pembrolizumab (MK-3475) as monotherapy in the adjuvant treatment of renal cell carcinoma (RCC) post nephrectomy" that further describes the clinical benefit of pembrolizumab for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions. Provide an interim analysis for OS for the study milestones.

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

[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.

This completes all your postmarketing requirements (PMRs) and postmarketing commitments (PMCs) acknowledged in our November 17, 2021, 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 601.70 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]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Sherry Hou, PharmD, Senior Regulatory Project Manager, at 240-402-1813.

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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

[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

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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/

DANIEL L SUZMAN
08/07/2024 09:25:01 AM