BLA 125514/S-170

CORRECTED SUPPLEMENT APPROVAL/
FULFILLMENT OF A POSTMARKETING REQUIREMENT

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.
Attention: Anita Lalloo, PhD
Director, Global Regulatory Affairs
351 North Sumneytown Pike, P.O. Box 1000
UG-2D-044
North Wales, PA 19454-2505

Dear Dr. Lalloo:

Please refer to your July 24, 2024, supplemental biologics license application (sBLA) and your amendments, submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab), for injection.

This Prior Approval supplemental biologics license application provides updates to the Keytruda (pembrolizumab) Prescribing Information and traditional approval of Keytruda in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

We also refer to our March 18, 2025, approval letter in which the section entitled, "Subpart E Fulfilled" was inadvertently omitted, and a footnote in the Gastric Cancer section of Highlights of the Prescribing Information was included that was no longer applicable. This corrected action letter includes the "Subpart E Fulfilled" section, and the footnote in the Highlights Gastric Cancer section of the Prescribing Information that was removed. The effective action date will remain March 19, 2025, the date of the original letter.

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, 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, and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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 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).

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your July 18, 2024, submission containing the final report for the following postmarketing requirement (PMR) listed in the May 5, 2021, approval letter for BLA 125514/S-097.

4033-1 Submit the final progression-free survival and final overall survival analyses and datasets for the ongoing clinical trial KEYNOTE-811, "A Phase III, Randomized, Double-blind Trial Comparing Trastuzumab Plus Chemotherapy and Pembrolizumab With Trastuzumab Plus Chemotherapy and Placebo as First-line Treatment in Participants With

[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.

HER2 Positive Advanced Gastric or Gastroesophageal Junction Adenocarcinoma" to verify and describe the clinical benefit of pembrolizumab with trastuzumab plus chemotherapy for patients with HER2-positive advanced or metastatic gastric or gastroesophageal adenocarcinoma.

We have reviewed your submission and conclude that the above requirement was fulfilled. This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our May 5, 2021, approval letter.

You are not required to report on the status of closed (released or fulfilled) PMRs 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 601.12(f)(4)]. 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).

[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

If you have any questions, contact Gina Davis, Senior Regulatory Health Project Manager at Gina.Davis@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Steven Lemery, MD, MHS
Director
Division of Oncology 3
Office of Oncologic Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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/

STEVEN J LEMERY
04/03/2025 04:01:51 PM