BLA 125514/S-127

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Attention: Teja Munshi
Director, Global Regulatory Affairs
126 E. Lincoln Avenue, RY 34-B295
Rahway, NJ 07065

Dear Ms. Munshi:

Please refer to your February 25, 2022, supplemental biologics license application (sBLA), submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab), injection, 100 mg.

This Prior Approval supplemental biologics license application provides updates to the Keytruda (pembrolizumab) Prescribing Information with an alternate dosing regimen of 400 mg every six weeks for all approved adult solid tumor indications based upon data obtained from Cohort B of the KEYNOTE-555 Trial described in postmarketing requirement (PMR) 3850-1. Labeling for the alternative dosing regimen of 400 mg every six weeks for adult classical Hodgkin lymphoma and adult primary mediastinal large B cell lymphoma continue to state that these indications are approved under accelerated approval and that continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

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) 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 originally approved this supplemental BLA for an alternative dosing regimen of 400 mg every six weeks for adult patients 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 to support the alternative dosing regimen for adult solid tumor indications.

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.

[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

We have received your February 22, 2022, submission containing the final report for the following postmarketing requirement listed in the April 28, June 16, and June 24, 2020, approval letters for the following supplemental applications: 059, 062, 063, 069, 076, 077, 078, 079, 080, 082, 083, 090, and 092.

3850-1 Submit the final analysis of overall response rate, duration of response, and safety from Cohort B of the KEYNOTE-555 trial titled, "A Phase 1 Randomized Clinical Study of Pembrolizumab (MK-3475) to Evaluate the Relative Bioavailability of Subcutaneous Injection Versus Intravenous Infusion in Participants With Advanced Melanoma" to verify and describe the anticipated effects of the alternative dosing regimen for pembrolizumab 400 mg every six weeks, that may inform product labeling across indications. All responding patients should be followed for at least 12 months from the onset of response. Provide pharmacokinetic data at first cycle and at steady state from Cohort B and the datasets in the final report.

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 June 24, 2020, letter however there are postmarketing requirements listed in the April 28 and June 16, 2020, approval letters that are still open.

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]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

[3] For the most recent version of a guidance, check the FDA guidance web page athttps://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

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 Gina Davis, Senior Regulatory Health Project Manager at (301) 796-0704.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:

- Content of Labeling
  - Prescribing Information

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
12/16/2022 08:54:31 AM