BLA 125514/S-131

SUPPLEMENT APPROVAL /
FULFILLMENT OF
POSTMARKETING COMMITMENTS

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Attention: Geet Mankad
Director, Global Regulatory Affairs
126 E. Lincoln Avenue, RY34-B2133
Rahway, NJ 07065

Dear Mr. Mankad:

We acknowledge your May 4, 2022, 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 updates the Indications and Usage section to include the phrase "as determined by an FDA approved test" for the Microsatellite Instability-High or Mismatch Repair Deficient Cancer (subsection 1.7) and the Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (subsection 1.8) indications in the Keytruda prescribing information.

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).

FULFILLMENT OF POSTMARKETING COMMITMENTS

We have received your June 30, 2021, submissions containing the final reports for the following postmarketing commitments listed in the May 23, 2017, approval letter for BLA 125514/S-014.

3213-3 Commitment to support the availability through an appropriate analytical and clinical validation study using clinical trial data that will support labeling of an immunohistochemistry based *in vitro* diagnostic device that is essential to the safe and effective use of pembrolizumab for patients with tumors that are mismatch repair deficient.

3213-4 Commitment to support the availability through an appropriate analytical and clinical validation study using clinical trial data that will support labeling of a nucleic acid-based *in vitro* diagnostic device that is essential to the safe and effective use of pembrolizumab for patients with tumors that are microsatellite instability high.

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

[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.

We remind you that there are postmarketing requirements listed in the May 23, 2017, approval letter that are still open.

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.

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 (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

ENCLOSURE:

- Content of Labeling

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
06/21/2022 05:27:22 PM