BLA 125514/S-91 & S-93

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING COMMITMENTS

Merck Sharp & Dohme Corp.
Attention: William Kwok
Director, Regulatory Affairs
126 E. Lincoln Ave.
P.O. Box 2000, RY34-B293
Rahway, NJ 07065

Merck Sharp & Dohme Corp.
Attention: Robert Kester
Director, Regulatory Affairs
126 E. Lincoln Ave.
P.O. Box 2000, RY34-B295
Rahway, NJ 07065

Dear Mr. Kwok and Mr. Kester:

Please refer to your supplemental biologics license applications (sBLAs) dated and received June 11, 2020, and dated and received June 16, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab) injection, for intravenous use.

These Prior Approval supplemental biologics applications provide for the following:

S-91: Revision of the CLINICAL STUDIES section to provide mature overall survival (OS) data for KEYNOTE-189. Minor revision of progression-free survival (PFS) data for KEYNOTE-189 and KEYNOTE-42 as a result of medical imaging measurement discrepancies.

S-93: Revision of the CLINICAL STUDIES section to provide mature OS data for KEYNOTE-407. Minor revision of PFS data for KEYNOTE-407 as a result of medical imaging measurement discrepancies.

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 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).

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.

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[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 COMMITMENTS

Your submissions dated June 11, 2020 and June 16, 2020, contained the final reports for the following postmarketing commitments listed in the August 20, 2018, approval letter for BLA 125514/S-35 and the October 30, 2018, approval letter for BLA 125514/S-41:

3433-1 Submit the clinical trial report and datasets for the updated survival results for KEYNOTE-189, entitled "A Randomized, Double-Blind, Phase III Study of Platinum plus Pemetrexed Chemotherapy with or without Pembrolizumab (MK3475) in First Line Metastatic Non-squamous Non-small Cell Lung Cancer Subjects," in order to inform the label with mature overall survival data in accordance with the pre-specified final analysis of KEYNOTE-189.

3469-1 Submit the results of the final analysis of progression-free survival and overall survival data from KEYNOTE-407, entitled "A Phase 3 Study of Carboplatin-Paclitaxel/Nab-paclitaxel Chemotherapy with or without Pembrolizumab in First Line Metastatic Squamous Non-Small Cell Lung Cancer," to further characterize the efficacy and benefit:risk assessment of pembrolizumab, administered in combination with carboplatin and paclitaxel or nanoparticle albumin bound paclitaxel (nab-paclitaxel), and for inclusion in product labeling.

This completes all of your postmarketing commitments acknowledged in our August 20, 2018 and October 30, 2018, supplement approval letters.

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, please email Sharon Sickafuse, Senior Regulatory Health Project Manager, at sharon.sickafuse@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Harpreet Singh, M.D.
Director
Division of Oncology 2
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/

B HARPREET SINGH
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