



BLA 125554/S-099

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
COMMITMENT**

Bristol-Myers Squibb Company
ATTN: Noemi C. Guma, Ph.D.
Director - US Regulatory Lead, Global Regulatory Strategy & Policy
P.O. Box 5326
Princeton, NJ 08543

Dear Dr. Guma:¹

Please refer to your supplemental biologics license application (sBLA), dated and received March 19, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Opdivo (nivolumab) injection.

We also refer to our March 3, 2021, Supplement Request letter to revise the product label with the final overall survival (OS) results from clinical trial CA209238.

This Prior Approval supplemental biologics application provides for an update of Section 14 Clinical Studies, Adjuvant Treatment of Melanoma, subsection 14.2 of the U.S. Prescribing Information (PI) with the final OS results from clinical Trial CA209238.

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

¹ 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>.

[21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,² 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*.³

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.

FULFILLMENT OF POSTMARKETING COMMITMENT

We have received your submission dated September 22, 2020, containing the final report for the following postmarketing commitment listed in the December 20, 2017, approval letter for sBLA 125554/S-055.

- 3313-1 Submit the final clinical report and datasets at the time of the final analysis for overall survival (OS) of Trial CA209238, entitled “A Phase 3, Randomized, Double-blind Study of Adjuvant Immunotherapy with Nivolumab versus Ipilimumab after Complete Resection of Stage IIIB/C or

² <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

³ 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>.

Stage IV Melanoma in Subjects who are at High Risk for Recurrence (CheckMate 238)", to revise the product label with mature OS data.

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

This completes all of your postmarketing commitments acknowledged in our December 20, 2017, letter.

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*.⁴

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.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4).

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).

⁴ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁶ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

If you have any questions, call Maryam Khazraee, Regulatory Health Project Manager, at 301-796-7119.

Sincerely,

{See appended electronic signature page}

Steven Lemery, M.D., M.H.S.
Director (Acting)
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
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