



BLA 761097/S-009

ACCELERATED APPROVAL

Regeneron Pharmaceuticals, Inc.
Attention: Laura Simpson, Ph.D.
Senior Director, Regulatory Affairs
777 Old Saw Mill River Road
Tarrytown, NY 10591

Dear Dr. Simpson:

Please refer to your supplemental biologics license application (sBLA), dated and received September 3, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Libtayo (cemiplimab-rwlc) injection.

We also refer to our January 21, 2021, electronic mail (email) communication, wherein we notified you that we planned to administratively split BLA 761097/S-008, with the proposed indication of "LIBTAYO is indicated for the treatment of patients with locally advanced or metastatic basal cell carcinoma (BCC) previously treated with a hedgehog pathway inhibitor," into the following two supplements:

- BLA 761097/S-008: LIBTAYO is indicated for the treatment of patients with locally advanced basal cell carcinoma previously treated with a hedgehog pathway inhibitor.
- BLA 76097/S-009: LIBTAYO is indicated for the treatment of patients with metastatic basal cell carcinoma previously treated with a hedgehog pathway inhibitor.

This Prior Approval supplemental biologics application provides for a new indication for cemiplimab-rwlc, for the treatment of patients with metastatic basal cell carcinoma (mBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 601.41), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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, Patient Package Insert and Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effectuated” (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 Effectuated” (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).

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 601.41, require further adequate and well-controlled clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trial with due diligence. If postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 601.43(b), withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated January 29, 2021. This requirement, along with required completion dates, is listed below.

This postmarketing clinical trial is subject to the reporting requirements of 21 CFR 601.70:

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 at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

- 4012-1 Submit the report and datasets for the 53 patients with metastatic basal cell carcinoma (mBCC) from clinical study R2810 ONC 1620 evaluating objective response rate and duration of response, to verify and describe the clinical benefit of cemiplimab in patients with mBCC who experienced progression of disease on hedgehog pathway inhibitor therapy or were intolerant of prior hedgehog pathway inhibitor therapy. To further characterize the magnitude and durability of responses in patients with mBCC, all patients will have the opportunity for 57 weeks of follow-up following completion of cemiplimab-rwlc.

Final Protocol Submission:	04/2021
Primary Analysis Completion (mBCC):	05/2021
Final Report Submission:	02/2022

Submit clinical protocols to your IND 127100 for this product. In addition, under 21 CFR 601.70 you should include a status summary of each requirement in your annual report to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial.

Submit final reports to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated “**Subpart E Postmarketing Requirement(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.

We are waiving the pediatric study(ies) requirement for this application because necessary studies are impossible or highly impracticable.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 4012-2 Submit the final analysis of objective response rate and duration of response for the 53 patients with metastatic basal cell carcinoma (mBCC) from clinical study R2810 ONC 1620, in order to further characterize the durability of response in this cohort. For the analysis, all patients will have

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the opportunity for at least 1.5 years of follow-up following completion of cemiplimab-rwlc treatment. The study results may inform product labeling.

The timetable you submitted on January 29, 2021, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	04/2021
Trial Completion:	08/2023
Final Report Submission:	05/2024

Submit the datasets with the final report.

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 127100 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,” “**Postmarketing Commitment Final Report**,” or “**Postmarketing Commitment Correspondence**.”

PROMOTIONAL MATERIALS

Under 21 CFR 601.45, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 601.45, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

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

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, contact Leah Her, Senior Regulatory Health Project Manager, at (240) 402-6611 or leah.her@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Lola Fashoyin-Aje, M.D., M.P.H.
Deputy Director
Division of Oncology 3
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Medication Guide

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

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/

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