

NDA 210868/S-004

**SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT**

Pfizer Inc.
Attention: Ann Carey
Senior Director, Pfizer Global Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Ms. Carey:

Please refer to your supplemental new drug application (sNDA) dated and received October 30, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lorbrena (lorlatinib) tablets.

This Prior Approval sNDA provides for modifications to the November 2, 2018 approved indication, under the provisions of 21 CFR 314.510, for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on crizotinib and at least one other ALK inhibitor for metastatic disease; or alectinib as the first ALK inhibitor therapy for metastatic disease; or ceritinib as the first ALK inhibitor therapy for metastatic disease. Specifically, these modifications remove the following:

- the restriction for use only in patients whose disease has progressed on crizotinib and at least one other ALK inhibitor for metastatic disease; or alectinib or ceritinib as the first ALK inhibitor therapy for metastatic disease
- the statements that “This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.”

The updated indication based on this sNDA has been expanded “for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.” Revisions to the Prescribing Information and Patient Package Insert were also made for consistency with the expanded indication, and based on the results of the clinical trial verifying the clinical benefit of lorlatinib in this population.

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.

We note that your March 3, 2021 and March 2, 2021, submissions include final printed labeling (FPL) for your Prescribing Information and Patient Package Insert, respectively. We have not reviewed this FPL. You are responsible for assuring that the wording in this FPL is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

WAIVER OF 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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] 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).

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>.

SUBPART H FULFILLED

We approved NDA 210868 under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your requirement made under 21 CFR 314.510.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated October 30, 2020, reporting on the following postmarketing requirement listed in the November 2, 2018, approval letter:

- 3500-1 Conduct and submit the results of at least one multicenter, randomized clinical trial that verifies and describes the clinical benefit of lorlatinib in patients with locally advanced or metastatic non-small cell lung cancer without a history of prior systemic therapy for advanced disease and whose tumors harbor anaplastic lymphoma kinase (ALK) gene arrangement.

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

We remind you that there are postmarketing requirements listed in the November 2, 2018, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 4031-1 Submit the clinical study report and datasets for the final analysis of overall survival, planned to occur after a total of 198 events, for Study B7461006, "A Phase 3, Randomized, Open-Label Study of Lorlatinib Monotherapy versus Crizotinib Monotherapy in the First-line Treatment of

Patients with Advanced ALK-Positive Non-Small Cell Lung Cancer.” The final results of these analyses may inform product labeling.

The timetable you submitted on February 25, 2021, states that you will conduct this trial according to the following schedule:

Final Protocol Submission: 10/2019
Trial Completion: 12/2028
Final Report Submission: 06/2029

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

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Idara Udoh, Senior Regulatory Health Project Manager, at 301-796-3074.

Sincerely,

{See appended electronic signature page}

Martha Donoghue, M.D.
Deputy Director (Acting)
Division of Oncology 2 (DO2)
Office of Oncologic Diseases (OOD)
Center for Drug Evaluation and Research

³ For the most recent version of a guidance, check the FDA guidance web page at <https://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>

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

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/

MARTHA B DONOGHUE
03/03/2021 04:18:21 PM