NDA 210868/S-002

SUPPLEMENT APPROVAL

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 July 22, 2020, received July 22, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LORBRENA (lorlatinib) tablets.

This Prior Approval supplemental new drug application provides revisions and additions to the following subsections of the LORBRENA (lorlatinib) U.S. Prescribing Information (USPI), based on data from Study B7461026, entitled "A Phase 1, Open-Label, Fixed Sequence, 2-Period Study to Investigate the Effect of Multiple Doses of Modafinil on the Pharmacokinetics of Single Dose Lorlatinib (PF-06463922) in Healthy Participants":

- Concomitant Use of Strong CYP3A Inducers (2.3), Concomitant Use of Moderate CYP3A Inducers (2.4), and Dosage Modification for Strong CYP3A Inhibitors (2.5) in DOSAGE AND ADMINISTRATION,
- Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers (5.1) and Central Nervous System Effects (5.2) in WARNINGS AND PRECAUTIONS,
- Clinical Trials Experience (6.1) in ADVERSE REACTIONS,
- Effect of Other Drugs on LORBRENA (7.1) and Effect of LORBRENA on Other Drugs (7.2) in DRUG INTERACTIONS,
- Hepatic Impairment (8.6) and Renal Impairment (8.7) in USE IN SPECIFIC POPULATIONS, and
- Pharmacodynamics (12.2) and Pharmacodynamics (12.3) in CLINICAL PHARMACOLOGY.

Additionally, updates were made to the Patient Package Insert.

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 January 22, 2021, submission includes final printed labeling (FPL) for your Prescribing Information and Patient Package Insert. 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.

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).

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

[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.

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.

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}

Meredith K. Chuk, M.D.
Supervisory Associate Director for Safety
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[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

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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/

MEREDITH K CHUK
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