NDA 213246/S-002

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT

Loxo Oncology, Inc., a wholly owned subsidiary of Eli Lilly and Company
c/o Eli Lilly and Company
Attention: James A. Lesueur, Ph.D.
Advisor, Global Regulatory Affairs – North America
Lilly Corporate Center, Drop Code 2543
Indianapolis, IN 46285

Dear Dr. Lesueur:

Please refer to your supplemental new drug application (sNDA) dated September 21, 2020, received September 21, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for RETEVMO (selpercatinib) capsules.

This Prior Approval supplemental new drug application provides for additions and revisions to the following sections of the package insert, which also includes results from renal impairment study LOXO-RET-18023, entitled "A Phase 1, Open-Label, Parallel-Cohort, Single-Dose Study to Evaluate the Effect of Renal Impairment on the Pharmacokinetics of LOXO-292":

- Hypersensitivity (5.5) and Tumor Lysis Syndrome (5.6) in WARNINGS AND PRECAUTIONS
- Clinical Trials Experience (6.1) in ADVERSE REACTIONS
- Pediatric Use (8.4) and Renal Impairment (8.6) in USE IN SPECIFIC POPULATIONS
- DESCRIPTION (11)
- Mechanism of Action (12.1) and Pharmacokinetics (12.3) in CLINICAL PHARMACOLOGY
- Carcinogenesis, Mutagenesis, Impairment of Fertility (13.1) in NONCLINICAL TOXICOLOGY
- Metastatic RET Fusion-Positive Non-Small Cell Lung Cancer (14.1) and RET-Mutant Medullary Thyroid Cancer (14.2) in CLINICAL STUDIES
- HOW SUPPLIED/STORAGE AND HANDLING (16), and
- PATIENT COUNSELING INFORMATION (17).

Also, updates were made to the Patient Package Insert to include the addition of tumor lysis syndrome in the *"What are the possible side effects of RETEVMO?"* section.

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 25, 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).

[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.

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.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated July 17, 2020, containing the final report for the following postmarketing requirement listed in the May 8, 2020, approval letter:

3829-8 Submit the analysis and datasets with the final report from an ongoing renal impairment clinical trial to evaluate the pharmacokinetics and safety of selpercatinib in patients with normal renal function and patients with renal impairment. Design and conduct the trial in accordance with the FDA Guidance for Industry titled "*Pharmacokinetics in Patients with Impaired Renal Function: Study Design, Data Analysis, and Impact on Dosing and Labeling*."

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

We remind you that there are postmarketing requirements and postmarketing commitments listed in the May 8, 2020, approval letter that are still open.

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]

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

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}

Harpreet Singh, M.D.
Director
Division of Oncology 2 (DO2)
Office of Oncologic Diseases (OOD)
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[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/

B HARPREET SINGH
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