NDA 213246/S-017
NDA 218160/S-007

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENT

Eli Lilly and Company
Attention: Nancy C Cress, B. Sc.
Director, Global Regulatory Affairs
Lilly Corporate Center
Drop Code 2543
Indianapolis, IN 46285

Dear Nancy Cress:

Please refer to your supplemental new drug applications (sNDAs) dated and received November 12, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Retevmo (selpercatinib) capsules and tablets.

These Prior Approval sNDAs provide for conversion from accelerated approval to traditional approval of Retevmo (selpercatinib) for the treatment of adult and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a RET gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options.

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.

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 and 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.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Information on submitting SPL files using eList may be found in 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).

SUBPART H FULFILLED

We approved this NDA 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 commitments made under 21 CFR 314.510.

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 none of these criteria apply to your supplemental applications, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submission dated November 12, 2025, containing the final report for the following postmarketing requirements listed in the September 21, 2022, and May 29, 2024, approval letters.

4342-1 Complete clinical trial(s) to obtain data on the clinical efficacy of selpercatinib through more precise estimation of the overall response rate and mature response duration per independent review assessment, in at

[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.

least 60 patients with locally advanced or metastatic RET-fusion positive solid tumors other than non-small cell lung cancer and thyroid cancer, who have progressed on prior systemic treatment or have no satisfactory alternative treatment options. A sufficient number of patients with tumor types for which responses require additional characterization (e.g., colorectal cancer, esophagogastric cancer, and glioma) will be evaluated. Overall response rate and duration of response will be assessed by independent central review and all responding patients will be followed for at least 12 months following the onset of response or until disease progression or death or early treatment discontinuation, whichever comes first. Include available data regarding RET fusion partners and co-occurring genetic alterations for all patients.

4639-3 Complete clinical trial(s) to obtain data on the clinical efficacy of selpercatinib through more precise estimation of the overall response rate and mature response duration per independent review assessment, in at least 60 patients with locally advanced or metastatic RET-fusion positive solid tumors other than non-small cell lung cancer and thyroid cancer, who have progressed on prior systemic treatment or have no satisfactory alternative treatment options. A sufficient number of patients with tumor types for which responses require additional characterization (e.g., colorectal cancer, esophagogastric cancer, and glioma) will be evaluated. Overall response rate and duration of response will be assessed by independent central review and all responding patients will be followed for at least 12 months following the onset of response or until disease progression or death or early treatment discontinuation, whichever comes first. Include available data regarding RET fusion partners and co-occurring genetic alterations for all patients.

We have reviewed your submission and conclude that the above requirements were fulfilled.

This closes all of your postmarketing requirements and postmarketing commitments acknowledged in our September 21, 2022, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 314.81(b)(2)(vii).

We remind you that there is a postmarketing requirement listed in the May 29, 2024, approval letter that is still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see

guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*

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.[3] Information and Instructions for completing the form can be found at FDA.gov.[4]

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

[3] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, email Maritsa Stephenson, PharmD, BCPS, Regulatory Health Project Manager, at maritsa.stephenson@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Nicole Drezner, M.D.
Deputy Director
Division of Oncology 2
Office of Oncologic Diseases
Center for Drug Evaluation and Research

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/

NICOLE L DREZNER
07/14/2026 01:00:30 PM