CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218160Orig1s000

SUMMARY REVIEW

Labeling Supplement – Clinical Review

Application Type (NDA/BLA)	NDA
Application Number(s)/ supplement number	218160
Received Date	June 13, 2023
PDUFA Goal Date	April 13, 2024
Review Completion Date	*Electronic stamp date*
Division/Office	Division of Oncology 2
Medical Officer	Elizabeth Duke
Team Leader	Diana Bradford
Associate Director for Labeling	Barbara Scepura
Deputy Division Director	Nicole Drezner
Product: Established Name (Trade name)	Selpercatinib (RETEVMO)
Formulation	Tablet
Applicant	Loxo Oncology, a wholly owned subsidiary of Eli Lilly and Company (Lilly)
Recommended Regulatory Action	Traditional Approval

1. Executive Summary:

Selpercatinib (RETEVMO) is an oral kinase inhibitor, originally approved on May 8, 2020 for the treatment of certain patients with *RET*-activated solid tumors. The currently approved formulation is capsules (40 mg and 80 mg strengths).

On June 13, 2023, Lilly submitted NDA 218160 for an immediate-release, film-coated tablet formulation of selpercatinib in strengths of 40, 80, 120, and 160 mg, including bioequivalence data comparing the tablet formulation with the commercial capsule formulation. The Applicant stated the tablet formulation was developed to minimize the size of the dosage form as well as the quantity of dosage units a given patient would be required to take relative to the commercial capsule formulation (e.g., to administer a 160 mg dose, one tablet versus two 80 mg capsules would be required). The indications for the tablet formulation are unchanged from those approved for use with the commercial capsule formulation.

There were no new clinical patient data submitted with this application. The review team determined that based on the overall benefit:risk profile of selpercatinib in previously reviewed clinical studies and the additional clinical pharmacology studies submitted in NDA 218160, the submitted data meet criteria for approval.

2. Regulatory History

Selpercatinib is a kinase inhibitor indicated for the treatment of:

- Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection (RET) gene fusion, as detected by an FDA-approved test
- Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, as detected by an FDA-approved test, who require systemic therapy[1]
- Adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a RET gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)[1]
- Adult patients with locally advanced or metastatic solid tumors with a RET gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options[1]

[1] This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

The recommended dosage of selpercatinib in adults and pediatric patients 12 years of age or older is based on weight:

- Less than 50 kg: 120 mg orally twice daily
- 50 kg or greater: 160 mg orally twice daily

3. Background and Review of Clinical Data

No additional clinical patient data were submitted in support of this application.

The tablet formulation was evaluated in 2 clinical studies in healthy participants:

- **J2G-MC-JZJZ (JZJZ):** Open-label, randomized, 2-period, 2-formulation, 2-sequence, 2-stagea adaptive crossover study to evaluate **bioequivalence** of a single 160-mg dose of selpercatinib as the tablet formulation compared with 2 x 80-mg commercial capsule formulation
- **J2G-MC-JZPA (JZPA):** Open-label, randomized, 2-period, 2-sequence crossover study in the fed and fasted states to assess the **effect of food** on the PK profile of selpercatinib after a high-fat meal

The application is based on the overall benefit:risk profile of selpercatinib in previously reviewed clinical studies and the additional clinical pharmacology studies submitted in NDA 218160.

Refer to the original multi-disciplinary review under NDA 213246 dated May 8, 2020, as well as efficacy supplements 7 and 8 (dated September 21, 2022), for a description and review of the clinical data.

4. Labeling changes

A summary of labeling changes is presented in Table 1.

Table 1: Summary of Labeling Changes (adapted from submission)

Section	Key Updates
2.3 Recommended Dosage	Added "Swallow the tablets whole. Do no crush or chew the tablets."
3. Dosage Forms and Strengths	Added information regarding the characteristics of selpercatinib tablets (40 mg, 80 mg, 120 mg, 160 mg)
11. Description	Added section on tablet formulation including composition and active ingredients in the tablet
12.3 Pharmacokinetics	Added statement "The capsule and tablet dosage forms of selpercatinib are bioequivalent."
16. How Supplied	Added information on tablet formulation

5. Financial Disclosures

Financial disclosure information was provided for all principal investigators and subinvestigators who participated at sites that enrolled patients for Study JZJZ. Financial disclosure information was not provided for Study JZPA as it was not considered a covered clinical study.

Covered Clinical Study (Name and/or Number):* An Open-Label, Randomized Study to Evaluate the Bioequivalence of Selpercatinib Formulations (J2G-MC-JZJZ or JZJZ)

Was a list of clinical investigators provided:	Yes ☒	No ☐ (Request list from Applicant)
Total number of investigators identified: 20		
Number of investigators who are Sponsor employees (including both full-time and part-time employees): 0		
Number of investigators with disclosable financial interests/arrangements (Form FDA 3455): 0		
If there are investigators with disclosable financial interests/arrangements, identify the number of investigators with interests/arrangements in each category (as defined in 21 CFR 54.2(a), (b), (c) and (f)): Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: _____ Significant payments of other sorts: _____		

Proprietary interest in the product tested held by investigator: _____ Significant equity interest held by investigator in study: _____ Sponsor of covered study: _____		
Is an attachment provided with details of the disclosable financial interests/arrangements:	Yes ☐	No ☐ (Request details from Applicant) ☒Not applicable given 0 investigators with disclosable financial interests/arrangements
Is a description of the steps taken to minimize potential bias provided:	Yes ☐	No ☐ (Request information from Applicant) ☒Not applicable given 0 investigators with disclosable financial interests/arrangements
Number of investigators with certification of due diligence (Form FDA 3454, box 3) 0		
Is an attachment provided with the reason:	Yes ☐	No ☐ (Request explanation from Applicant) ☒Not applicable given 0 investigators with disclosable financial interests/arrangements

Abbreviation: CFR = Code of Federal Regulations.

6. Recommended Regulatory Action

The clinical review team recommends approval of NDA 218160 as summarized in this review and upon satisfactory review from other FDA disciplines.

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/

ELIZABETH S DUKE
04/09/2024 03:28:31 PM

DIANA L BRADFORD
04/09/2024 03:29:35 PM

NICOLE L DREZNER
04/09/2024 03:33:14 PM