

NDA 214096/S-001
NDA 214096/S-002

SUPPLEMENT APPROVAL

EMD Serono, Inc.
Attention: Srinivas Patchala
Director, Global Regulatory Affairs-Oncology
45A Middlesex Turnpike
Billerica, MA 01821

Dear Mr. Patchala:

Please refer to your supplemental new drug applications (sNDAs) dated and received on September 23, 2022 [for supplement 1 (S-001)] and October 21, 2022 [for supplement 2 (S-002)], and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TEPMETKO (tepotinib) tablets.

These Prior Approval sNDAs provide for the following updates to the US Prescribing Information and Patient Information labeling for TEPMETKO (tepotinib):

S-001

Revisions to the DOSAGE AND ADMINISTRATION section (2. 3, *Administration to Patients Who Have Difficulty Swallowing Solids*) and Patient Information to allow alternative methods of TEPMETKO tablets administration via oral drinking suspension or nasogastric feeding tubes, based on the available pharmacokinetic and CMC data

S-002

Revisions to the DRUG INTERACTIONS (7) and CLINICAL PHARMACOLOGY (12) sections, as specified below, based on the results of clinical pharmacology studies MS200095-0051 and MS200095-0053, and fulfilling Postmarketing Requirements and Commitments 4013-2 and 4013-3 included in the February 3, 2021 Accelerated Approval letter.

- Deletion of “Effects of Other Drugs on TEPMETKO” from subsection 7.1
- Modifications to “Drug Interaction Studies” in subsection 12.3

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, Patient Package Insert), with the addition of any labeling changes in pending “Changes Being Effectuated” (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 the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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>.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submission dated July 28, 2022 and September 26, 2022, containing the final reports for the following postmarketing requirement and commitment listed in the February 3, 2021, approval letter.

- 4013-2 Conduct a drug interaction study to evaluate the effect of itraconazole on the single dose pharmacokinetics of tepotinib to assess the magnitude of increased drug exposure and determine appropriate dosing recommendations when tepotinib is administered concomitantly with a strong CYP3A4 and P-gp inhibitors. Design and conduct the study in accordance with the FDA Guidance for Industry titled “Clinical Drug Interaction Studies —Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions.”
- 4013-3 Conduct a drug interaction study to evaluate the effect of rifampin on the single dose pharmacokinetics of tepotinib to assess the magnitude of decreased drug exposure and determine appropriate dosing recommendations when tepotinib is administered concomitantly with a strong CYP3A4 inducer and moderate CYP2C8 inducer. Design and conduct the trial in accordance with the FDA Guidance for Industry titled “Clinical Drug Interaction Studies —Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions.”

We have reviewed your submissions and conclude that the above requirement and commitment were fulfilled.

We remind you that there is a postmarketing requirement and a postmarketing commitment listed in the February 3, 2021, approval letter that are still open.

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

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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).

If you have any questions, contact Jacqueline Glen, Regulatory Health Project Manager, at Jacqueline.Glen@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Erin Larkins, M.D.
Supervisory Associate Director
Division of Oncology 2
Office of Oncologic Diseases
Office of New Drugs
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/

ERIN A LARKINS
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