



NDA 204114/S-021

**SUPPLEMENT APPROVAL/  
FULFILLMENT OF POSTMARKETING REQUIREMENT**

Novartis Pharmaceuticals Corporation  
Attention: Carolyn Zhu, Pharm.D.  
Global Program Regulatory Manager  
Regulatory Affairs, Oncology  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Dr. Zhu:

Please refer to your supplemental new drug application (sNDA) dated and received July 30, 2021, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Mekinist (trametinib) tablets.

This Prior Approval labeling supplement (sNDA) provides the following changes for the Mekinist (trametinib) Prescribing Information (PI): to update Section 8.6 Hepatic Impairment and Section 12.3 Pharmacokinetics, based on the final study report for Protocol NCI-9591 (PJC-015) entitled, "A Phase I Trial of Single Agent Trametinib (GSK1120212) in Advanced Cancer Patients with Hepatic Dysfunction," associated with PMR 2045-3. This supplement also includes additional minor editorial revisions.

**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.

**WAIVER OF HIGHLIGHTS ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

**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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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.

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*.<sup>2</sup>

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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

### **FULFILLMENT OF POSTMARKETING REQUIREMENT**

We have received your submission dated July 30, 2021, containing the final report for the following postmarketing requirement listed in the May 29, 2013, approval letter.

- 2045-3 Conduct a pharmacokinetic trial to determine the appropriate dose of Mekinist (trametinib) in patients with hepatic impairment in accordance with the FDA Guidance for Industry entitled “Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling.”

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<sup>2</sup> 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>.

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

We remind you that there is a postmarketing requirement listed in the May 29, 2013, approval that is still open.

### **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 Kristin Jarrell, Pharm.D., Regulatory Health Project Manager, at (301) 796-0137.

Sincerely,

*{See appended electronic signature page}*

Steven Lemery, MD, M.H.S.  
Director (Acting)  
Division of Oncology 3  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

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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.**  
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/s/  
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STEVEN J LEMERY  
01/28/2022 02:35:45 PM