



NDA 021877/S-009

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING COMMITMENT**

Novartis Pharmaceuticals Corporation  
Attention: Luz Patricia Lee  
Senior Associate Director, Regulatory Affairs  
One Health Plaza  
Ease Hanover, NJ 07936-1080

Dear Ms. Lee:

Please refer to your Supplemental New Drug Application (sNDA) dated August 31, 2018, received August 31, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ARRANON<sup>®</sup> (nelarabine) Intravenous Injection, 250 mg/50 mL.

This Prior Approval supplemental new drug application provides for updates to the Boxed Warning and Warnings and Precautions sections regarding Neurologic Adverse Reactions and provides for fulfillment of PMC 3447-1.

**APPROVAL & LABELING**

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

<http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

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.

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 August 31, 2018, containing the final report for the following postmarketing commitment listed in the July 3, 2018 supplement 008 approval letter for this application:

PMC 3447-1 Characterize the neurological adverse reactions to nelarabine with regard to time to onset, maximum grade and duration. Submit a description of the results of the analysis, data files used to perform the analysis, and labeling updated with the additional information about the characteristics of the neurological adverse reactions.

The timetable you submitted on June 29, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission 8/31/2018

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

This completes all of your postmarketing commitments acknowledged in our July 3, 2018, letter.

We remind you that there is a postmarketing requirement listed in the October 28, 2005 approval letter that is still open.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

### **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 Natasha Kormanik, Regulatory Health Project Manager, at (240) 402-4227.

Sincerely,

{See appended electronic signature page }

Barry W. Miller, MS, CRNP  
Acting Deputy Director for Safety  
Division of Hematology Products  
Office of Hematology and Oncology Products  
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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BARRY W MILLER  
11/29/2018