



NDA 212526/S-007

**SUPPLEMENT APPROVAL/  
FULFILLMENT OF POSTMARKETING  
COMMITMENTS**

Novartis Pharmaceuticals Corporation  
Attention: Sadia Afrin, MS  
Global Program Regulatory Manager  
Regulatory Affairs, Oncology  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Ms. Afrin:

Please refer to your supplemental new drug application (sNDA) dated January 28, 2022, received January 28, 2022, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for PIQRAY® (alpelisib), 50 mg, 150 mg, and 200 mg tablets.

This Prior Approval supplemental new drug application provides for the following changes:

- Updates to the U.S. prescribing information to include the final overall survival data from study BYL719C2301 (SOLAR-1)
- Updates to the Drug Interactions subsection 7.1, Clinical Pharmacology subsection 12.3 and Patient Counseling section 17, based on results from drug-drug interaction study BYL719A2110
- Updates to the Nonclinical Toxicology subsection 13.1 to include data from nonclinical fertility toxicology studies 2070119 and 2070120

**APPROVAL & LABELING**

We have completed our review of this application. 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.<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 Medication Guide), 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 the FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(I)(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 COMMITMENTS**

We have received your submission dated January 27, 2022, containing the final report for 3573-1, and your submission dated January 28, 2022, reporting on 3573-2, for the following postmarketing commitments listed in the May 24, 2019, approval letter.

- 3573-1 Submit the final overall survival (OS) analysis and datasets with the final report from the ongoing clinical trial BYL719C2301, SOLAR-1, entitled “A Phase III randomized double-blind, placebo controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer with progressed on or after aromatase inhibitor treatment.”

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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>.

- 3573-2 Conduct a clinical trial to evaluate the effect of repeat doses of a strong CYP3A inducer on pharmacokinetics of alpelisib to assess the magnitude of decreased alpelisib exposure and to determine appropriate dosing recommendations. Design and conduct the trial in accordance with the FDA Guidance for Industry; "Clinical Drug Interaction Studies- Study Design, Data Analysis, and Clinical Implications."

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

We remind you that there is a postmarketing commitment listed in the May 24, 2019, 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 the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>3</sup>

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.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup>

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-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related 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).

### **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 the 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

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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 the 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, call Zohal Hamidi, Regulatory Project Manager, at 301-796-6383.

Sincerely,

*{See appended electronic signature page}*

Laleh Amiri-Kordestani, MD  
Director  
Division of Oncology 1  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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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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LALEH AMIRI KORDESTANI  
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