NDA 209092/S-005
NDA 209935/S-008

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING COMMITMENT

Novartis Pharmaceuticals Corporation
Attention: Colin Vechery, PharmD
Senior Global Program Regulatory Manager
Regulatory Affairs, Oncology Business Unit
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Vechery:

Please refer to the following supplemental new drug applications (sNDAs) and their amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA):

> NDA 209092/S-005 dated December 6, 2019, received December 6, 2019, for Kisqali (ribociclib) tablets
>
> NDA 209935/S-008 dated December 19, 2019, received December 19, 2019, for Kisqali/Femara Co-pack (ribociclib tablets in combination with letrozole tablets)

Prior Approval supplement new drug application NDA 209092/S-005 provides for updates to Section 14 of the Full Prescribing Information (Clinical Studies) to add efficacy data from CLEE011F2301 (MONALEESA-3) to fulfill PMC 3453-2 from the July 18, 2018, approval letter for S-001.In addition, the Full Prescribing Information was updated to add a new Severe Cutaneous Adverse Reactions subsection to Section 5 (Warnings and Precautions) with information regarding toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Related updates were also made to Highlights, Section 2 (Dosage and Administration), Section 6 (Adverse Reactions), and Section 17 (Patient Counseling Information).

Prior Approval supplemental new drug application NDA 209935/S-008, provides for the same updates as proposed in NDA 209092/S-005 for Kisqali.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are 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 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*.[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.

We are waiving the pediatric studies requirement for this application because necessary studies are impossible or highly impracticable in children. Breast cancer occurs, for the most part, in the adult population. The incidence of this cancer type in pediatric patients is extremely rare and as such, clinical pediatric studies are impossible or highly impracticable.

[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.

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

We refer to your supplemental new drug application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kisqali (ribociclib) tablets.

We have received your submission dated December 6, 2019, containing the *interim overall survival (OS) report* for the following postmarketing commitment listed in the July 18, 2018, approval letter for S-001.

3453-2 Submit the interim overall survival (OS) report with data and analysis; the final OS report with data and analysis, from clinical trial MONALEESA-3 entitled: "A randomized, double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with HR+, HER2 negative advanced breast cancer who have received no or only one line of prior endocrine treatment".

The timetable you submitted on July 13, 2018, states that you will conduct this study according to the following schedule:

Final protocol submission:	09/2016
Trial Completion:	09/2022
Interim OS report Submission:	09/2020
Final OS Report Submission:	03/2023

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

This completes all of your postmarketing commitments acknowledged in our July 18, 2018, approval letter for S-001.

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.*[3]

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

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.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

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 Rajesh Venugopal, Senior Regulatory Project Manager, at (301) 796-4730.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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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.

/s/

LALEH AMIRI KORDESTANI
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