DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 208573/S-004
NDA 208573/S-005

**SUPPLEMENT APPROVAL**
**FULFILLMENT OF POSTMARKETING REQUIREMENT**

AbbVie, Inc.
Attention: Tuah Jenta, PhD, RAC
Director, Regulatory Affairs
1 N. Waukegan Road
Dept. PA77/Bldg. AP30
North Chicago, IL 60064

Dear Dr. Jenta:

Please refer to your Supplemental New Drug Applications dated and received December 28, 2017 (S-004) and January 8, 2018 (S-005) and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for VENCLEXTA® (venetoclax); 10, 50 and 100 mg tablets.

These Prior Approval supplemental new drug applications provide for:

S-004: Confirmatory data to fulfill the Subpart H Post Marketing Requirement (PMR) 3068-1 involving Study GO28667/MURANO, "*A randomized, Phase 3 trial comparing VENCLEXTA® (venetoclax) and rituximab with bendamustine and rituximab in patients with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL), including CLL with deletion 17p*" for an indication approved under accelerated approval to receive regular approval.

S-005: Revision of monotherapy indication of VENCLEXTA® (venetoclax).

VENCLEXTA is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy.

## APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are 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 package insert 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 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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).

## SUBPART H FULFILLED

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of supplement S-004 fulfills your commitments made under 21 CFR 314.510.

## REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

## FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submissions dated December 28, 2017, containing the final report for the following postmarketing requirement listed in the April 11, 2016 approval letter.

PMR 3068-1 Submit the complete final report and data from trial GO28667, a randomized, Phase 3 trial comparing VENCLEXTA (venetoclax) and rituximab with bendamustine and rituximab in patients with relapsed or refractory chronic lymphocytic leukemia (CLL), including CLL with deletion 17p.

Study Completion: 05/2018
Final Report Submission: 05/2019

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 April 11, 2016 approval letter that is still open.

## POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments for supplement S-005:

PMC 3426-1 Provide updated efficacy information from Study M14-032 to characterize longer-term efficacy of venetoclax monotherapy in patients with previously treated chronic lymphocytic leukemia (CLL). Data will include independent review committee-assessed and investigator-assessed duration of response for all 127 patients with CLL with a shared cut-off date of March 30, 2018. Include a written summary and associated derived and tabulated datasets.

The timetable you submitted on May31, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2018

PMC 3426-2 Provide updated efficacy information from Study M12-175 to characterize longer-term efficacy of venetoclax monotherapy in patients with previously treated chronic lymphocytic leukemia (CLL) and small lymphocyte lymphoma (SLL). Data will include independent review committee-assessed and investigator-assessed duration of response for all 67 patients with CLL or SLL treated at the 400 mg dose, with a shared cut-off date of March 30, 2018. Include a written summary and associated derived and tabulated datasets.

The timetable you submitted on May 31, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/2019

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments 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 ).

You must submit final promotional materials and package insert(s), 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 http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

**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 Beatrice Kallungal, Regulatory Project Manager, at (301) 796-9304.

Sincerely,

*{See appended electronic signature page}*

R. Angelo de Claro, MD
Acting Deputy Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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ROMEO A DE CLARO
06/08/2018