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Approval Package for:

APPLICATION NUMBER:

NDA 205552 Orig1s002

Trade Name: **IMBRUVICA**

Generic or Proper Name: **ibrutinib**

Sponsor: **Pharmacyclics, Inc.**

Approval Date: **January 29th, 2015**

Indication: **Imbruvica is indicated for the treatment of paitents with Waldenstromös macroglobulinemia (WM)**

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NDA 205552 Orig1s002

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APPLICATION NUMBER:

205552Orig1s002

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205552/S-002

SUPPLEMENT APPROVAL
POST MARKETING FULFILLMENT

Pharmacyclics, Inc.
Attention: Christine Salido
Executive Director, Regulatory Affairs
995 East Arques Avenue
Sunnyvale, CA 94085-4521

Dear Ms. Salido:

Please refer to your Supplemental New Drug Application (sNDA) dated October 17, 2014, received October 17, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Imbruvica® (ibrutinib) capsules/140mg.

We acknowledge receipt of your amendments dated October 30; November 3, 7, 20, and 24 (2); December 2, 15, 22, and 23, 2014; and January 7 and 20, 2015.

This Prior Approval supplemental new drug application provides for a new indication for the treatment of patients with Waldenström's macroglobulinemia and fulfillment of the postmarketing requirement trial, PMR 2060-5, *"An Open-Label, Multicenter, Pharmacokinetic, Study of PCI-3265in Subjects with Varying Degrees of Hepatic Impairment"*.

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 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 includes 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).

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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2867-1 Develop and test the stability of a lower (35 or 70 mg) strength ibrutinib capsule in order to allow dose reductions for patients with moderate hepatic impairment for whom ibrutinib treatment is currently not recommended. The lower strength capsule should be sufficiently distinguishable from the 140 mg capsule.

The timetable you submitted on January 23, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/2015
Study Completion:	12/2016
Final Report Submission:	03/2017

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