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Approval Package for:

APPLICATION NUMBER:

205552Orig2s000

Trade Name:	Imbruvica
Generic Name:	Ibrutinib capsules, 140 mg
Sponsor:	Pharmacyclics, Inc.
Approval Date:	February 12, 2014
Indications:	For the treatment of patients with Chronic Lymphocytic Leukemia (CLL) who have received at least one prior therapy.

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APPROVAL LETTER

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205552/Original 2

ACCELERATED APPROVAL

Pharmacyclics, Inc.
Attention: Christine Salido
Executive Director, Regulatory Affairs
9995 East Arques Avenue
Sunnyvale, CA 94085-4521

Dear Ms. Salido:

Please refer to your New Drug Application (NDA) dated June 28, 2013, received June 28, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Imbruvica® (ibrutinib) capsules, 140 mg.

For administrative purposes we designated your originally submitted NDA as follows:

- NDA 205552/Original 1 – for the treatment of patients with Mantle Cell lymphoma (MCL). This indication was approved on November 13, 2013, under the provisions of accelerated approval regulations (21 CFR 314.500).
- NDA 205552/Original 2 – for the treatment of patients with Chronic Lymphocytic Leukemia (CLL) who have received at least one prior therapy.

The subject of this action letter is NDA 205552/Original 2.

We acknowledge receipt of your amendments dated May 6, 13, 2013; June 6, 20, 2013; July 12, 25(2), 26 (3), 30, 2013; August 1, 2 (7), 5 (2), 6, 7, 9, 12, 13 (3), 14 (11), 15, 16, 19, 20, 21, 23, 26, 29, 30, 2013; September 4, 6, 9 (3), 11, 12, 17 (2), 18, 23, 24, 25, 2013; October 1, 3 (2), 8, 11, 16 (3), 18, 23, 24, 29 (2), 31, 2013; November 5, 12, 13 (3), 15 (2), 18, 19 (6), 20 (2), 26 (3), 29, 2013; December 4 (2), 5, 12, 13 (5), 16, 17, 27, 2013; January 6, 7, 22, 2014; February 6, 7 (4), 10 and 11, 2014.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

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We note that your February 11, 2014, submission includes final printed labeling (FPL) for your package insert and patient package insert. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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, text for the patient package insert). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

ADVISORY COMMITTEE

Your application for Imbruvica® (ibrutinib) capsules, 140 mg was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues in the intended population.

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. You are required to conduct such studies/clinical trials with due diligence. If postmarketing studies/clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 314.530, withdraw this approval. We remind you of your postmarketing requirements specified in your submission dated, February 6, 2014. These requirements, along with required completion dates, are listed below.

PMR 2122-1:

Submit the results of the completed randomized, open-label Phase 3 clinical trial (PCYC-1112 CA) of ibrutinib versus ofatumumab in patients with relapsed or refractory chronic lymphocytic leukemia or relapsed or refractory small lymphocytic lymphoma. Enrollment of 391 patients was completed. The primary endpoint is progression-free survival as assessed by an Independent Review Committee.

Final Protocol Submission:	Completed (01/2014)
Trial Completion:	Completed (01/2014)
Final Report Submission:	06/2014

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