# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### *APPLICATION NUMBER:*

# 210563Orig1s000
# 210563Orig2s000

| | |
|---|---|
| ***Trade Name:*** | Imbruvica® tablets, 140 mg, 280 mg, 420 mg, and 560 mg. |
| ***Generic or Established:*** | ibrutinib |
| ***Sponsor:*** | Pharmacyclics LLC |
| ***Approval Date:*** | February 16, 2018 |
| ***Indication:*** | NDA 210563/Original 1 – Treatment of adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion, Waldenström's macroglobulinemia (WM), and chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.<br><br>NDA 210563/Original 2 – Treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy, and marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy. |

# CENTER FOR DRUG EVALUATION AND RESEARCH

# 210563Orig1s000
# 210563Orig2s000

## CONTENTS

## Reviews / Information Included in this NDA Review.

| | |
|---|---|
| **Approval Letter** | **X** |
| **Other Action Letters** | |
| **Labeling** | **X** |
| **REMS** | |
| **Summary Review** | **X** |
| **Officer/Employee List** | **X** |
| **Office Director Memo** | |
| **Cross Discipline Team Leader Review** | **X** |
| **Clinical Review(s)** | **X** |
| **Product Quality Review(s)** | **X** |
| **Non-Clinical Review(s)** | **X** |
| **Statistical Review(s)** | |
| **Clinical Microbiology / Virology Review(s)** | |
| **Clinical Pharmacology Review(s)** | **X** |
| **Other Reviews** | **X** |
| **Risk Assessment and Risk Mitigation Review(s)** | |
| **Proprietary Name Review(s)** | **X** |
| **Administrative/Correspondence Document(s)** | **X** |

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 210563Orig1s000
# 210563Orig2s000

# APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 210563/Original 1

**NDA APPROVAL**

Pharmacyclics LLC
Attention: Usha Ramesh, PhD
Executive Director, Regulatory Affairs
995 East Arques Avenue
Sunnyvale, CA 94085-4521

Dear Dr. Ramesh:

Please refer to your New Drug Application (NDA) dated August 31, 2017, received August 31, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Imbruvica® (ibrutinib) tablets, 140 mg, 280 mg, 420 mg, and 560 mg.

NDA 210563 provides for the use of Imbruvica® for the following indications which, for administrative purposes, we have designated as follows:

- NDA 210563/Original 1 – Treatment of adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion, Waldenström's macroglobulinemia (WM), and chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

- NDA 210563/Original 2 – Treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy, and marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy.

The subject of this action letter is NDA 210563/Original 1. A separate action letter will be issued for NDA 210563/Original 2.

## APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

## EXPIRATION DATING PERIOD

We grant a 24-month expiration period for the drug product when stored at controlled room temperature 20°C to 25°C (68°F to 77°F) with excursions permitted between 15°C and 30°C (between 59°F and 86°F).

## WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

## 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 (package insert and patient package insert). 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,* available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on February 14, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 210563**." Approval of this submission by FDA is not required before the labeling is used.

## 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.

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing

DOCKET ALARM

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

**LAW FIRMS**
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

**FINANCIAL INSTITUTIONS**
Litigation and bankruptcy checks for companies and debtors.

**E-DISCOVERY AND LEGAL VENDORS**
Sync your system to PACER to automate legal marketing.