CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 205-552/S-17

Trade Name:	Imbruvica
Generic Name:	ibrutinib capsules, 140 mg
Sponsor:	Pharmacyclics LLC.
Approval Date:	August 2, 2017
Indications:	For the treatment of patients with chronic graft-versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 205-552/S17

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	
Approvable Letter	
Labeling	
Summary Review	**X**
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	
Chemistry Review(s)	
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Other Review(s)	
Administrative/Correspondence Document(s)	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 205-552/S-17

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Ann. T. Farrell, M.D., Division Director
Subject	Division Director Summary Review
NDA/BLA # **Supplement #**	205552-017
Applicant Name	Pharmacyclics
Date of Submission	February 2, 2017
PDUFA Goal Date	August 2, 2017
Proprietary Name / **Established (USAN) Name**	Imbruvica/ibrutinib/PCI-32765
Dosage Forms / Strength	140 mg hard gelatin capsules
Proposed Indication(s)	Treatment of patients with chronic graft-versus host disease (cGVHD) after failure of one or more lines of systemic therapy
Action/Recommended Action for NME:	**Approval**

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	Tanya Wroblewski, M.D/R. Angelo de Claro, M.D.
Regulatory Health Project Manager	Esther Park, Pharm.D.
Statistical Review	Kallapa Koti, Ph.D./Lei Nie, Ph.D.
Pharmacology Toxicology Review	Luan Lee, Ph.D. / Christopher Sheth, Ph.D.
CMC Review/OBP Review	Pallaiah Thammana/Ramesh Raghavachari
Microbiology Review	N/A
Clinical Pharmacology Review	Liang Li, Ph.D./Stacy Shord, Ph.D.
DDMAC/OPDP	Nisha Patel/Kathleen Davis/Susan Redwood/Sharon R Mills/LaShawn Griffiths
OSI	Anthony Orencia, M.D./Janice Pohlman, M.D./Kassa Ayalew, M.D.
CDTL Review	Angelo deClaro, M.D.
OSE/DMEPA	Leeza Rahimi, Pharm.D./Yelena Maslov, Pharm. D.
COA Staff	Ebony Dashiell-Aje / Selena Daniels/Elecktra Papadopoulos, M.D.

Signatory Authority Review Template

1. Introduction

On November 13, 2013 Pharmacyclics, Inc. received approval for Imbruvica (ibrutinib). Ibrutinib (PCI-32765) is an irreversible inhibitor of Bruton's tyrosine kinase (Btk). Imbruvica is approved for treatment of patients with the following diseases:

Mantle cell lymphoma (MCL) who have received at least one prior therapy
Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) who have received at least one prior therapy
Chronic lymphocytic leukemia)/Small lymphocytic lymphoma (SLL) with 17p deletion
Waldenströms Macroglobulinemia
Marginal zone lymphoma

This submission provides for a new indication for the treatment of patients with chronic graft versus host disease (cGVHD), which is a serious and life-threatening condition occurring following hematopoietic stem cell transplant.

2. Background

There are no currently approved treatments for chronic graft versus host disease. Corticosteroids are the mainstay for the first-line treatment of cGVHD. There are no approved therapies for the treatment of cGVHD after failure of 1 or more lines of therapy.

From the CDTL review:
The primary basis for the application is clinical trial PCYC-1129-CA, titled "A Multicenter Open-Label Phase 1b/2 Study of Ibrutinib in Steroid Dependent or Refractory Chronic Graft Versus Host Disease" [Clinicaltrials.gov Identifier NCT02195869].

Formal meetings occurred between the Agency and the Applicant on 3 November 2015 and 31 August 2016 to discuss the development program and registration plans for Imbruvica to support an indication for the treatment of patients with chronic graft-versus-host disease.

FDA granted Breakthrough Therapy Designation for Imbruvica for the treatment of patients with cGVHD after failure of 1 or more lines of systemic therapy on 22 June

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.