

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.

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RESEARCH**

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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 #	205552-017
Supplement #	
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 Orenca, 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

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