CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210563Orig1s000
210563Orig2s000

SUMMARY REVIEW

Division Director Summary Review for Regulatory Action

Date	(electronic stamp)
From	R. Angelo de Claro, MD
Subject	Division Director Summary Review
NDA/BLA # and Supplement #	NDA 210563 (Type 3 NDA–New Dosage Form) Original-1 and Original-2
Applicant	Pharmacyclics, LLC
Date of Submission	31 August 2017
PDUFA Goal Date	28 February 2018
Proprietary Name	Imbruvica
Established or Proper Name	Ibrutinib
Dosage Form(s)	Tablets: 140mg, 280mg, 420mg and 560mg, for oral use
Applicant Proposed Indication(s)/Population(s)	Same indications as capsule dosage form
Action or Recommended Action:	*Approval*
Approved/Recommended Indication(s)/Population(s) (if applicable)	Same indications as capsule dosage form

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Medical Officer Review	Margret Merino / Tanya Wroblewski
Statistical Review	N/A
Pharmacology Toxicology Review	N/A
OPQ Review	Sherita McLamore (Application Technical Lead) / refer to CMC review for full list
Microbiology Review	N/A
Clinical Pharmacology Review	Liang Li / Olanrewaju Okusanya
OPDP	Nisha Patel
OSI	N/A
CDTL Review	Tanya Wroblewski
OSE/DEPI	N/A
OSE/DMEPA	N/A
OSE/DRISK	N/A
Other: Patient Labeling Review	Susan Redwood

Abbreviations: OND=Office of New Drugs, OPQ=Office of Pharmaceutical Quality, OPDP=Office of Prescription Drug Promotion OSI=Office of Scientific Investigations, CDTL=Cross-Discipline Team Leader, OSE= Office of Surveillance and Epidemiology DEPI= Division of Epidemiology, DMEPA=Division of Medication Error Prevention and Analysis, DRISK=Division of Risk Management

1. Benefit-Risk Assessment

The Applicant submitted a Type 3 NDA (new dosage form) to seek approval of a tablet dosage form with dose strengths of 140mg, 280 mg, 420mg, and 560mg. The tablets will have the same indications and dosing as the currently marketed ibrutinib capsules. The new tablet dosage forms are intended to improve pill burden and provide for appropriate doses with a single tablet.

Imbruvica capsule dosage form (NDA 205552) has regular approval for the following indications:

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

Imbruvica capsule dosage form (NDA 205552) has accelerated approval for the following indications:

- adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
- adult patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy

Regulatory Recommendation: Approval of NDA 210563 for the tablet dosage forms with dose strengths of 140 mg, 280 mg, 420 mg, and 560 mg for the same approved indications as for Imbruvica capsule dosage form (NDA 205552).

Accelerated approval (NDA 210563 Original-2) is recommended for the mantle cell lymphoma and marginal zone lymphoma indications because these indications remain under accelerated approval under NDA 205552. Regular approval (NDA 210563 Original-1) is recommended for all of the other indications.

2. Background

This application provides CMC and clinical pharmacology data to support stability and bioequivalence of a new tablet dosage form for ibrutinib. There was no new clinical efficacy or safety data included in this NDA and therefore no need for benefit-risk assessment. There are no updates to the indication, efficacy, or safety sections of the USPI.

3. Product Quality

From CMC Application Technical Lead Review:

*The Office of Pharmaceutical Quality (OPQ) recommends **APPROVAL** of NDA 210563 for IMBRUVICA® (ibrutinib) Tablets, 140 mg, 280 mg, 420 mg, 560 mg. As part of this action, OPQ grants a 24-month expiration period for the drug product when stored at 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). The Office of Pharmaceutical Quality has no Post-Marketing Commitments (PMCs) or Post-Marketing Requirements (PMRCs) to be conveyed to the applicant.*

No issues were identified that would preclude approval.

4. Nonclinical Pharmacology/Toxicology

No issues were identified that would preclude approval.

5. Clinical Pharmacology

From Clinical Pharmacology Review:

The Office of Clinical Pharmacology has reviewed the information submitted. The to-be-marketed tablet formulation at dose strengths of 140 mg, 280 mg, 420 mg, and 560 mg is considered approvable from a clinical pharmacology perspective. Dosing guidelines regarding food timings for ibrutinib tablets should follow the same recommendation for the ibrutinib capsules in the current labeling, i.e., there are no restrictions for food consumption when taking ibrutinib tablets or capsules.

No issues were identified that would preclude approval.

6. Clinical Microbiology

No issues were identified that would preclude approval.

7. Clinical/Statistical-Efficacy

No issues were identified that would preclude approval.

8. Safety

No new safety issues were identified that would preclude approval.

9. Advisory Committee Meeting

This product is not a new molecular entity.

10. Pediatrics

Ibrutinib has orphan drug designation for all of the approved indications and is thus exempt from pediatric study requirements described in 21 CFR 314.55.

11. Other Relevant Regulatory Issues

No issues were identified that would preclude approval.

12. Labeling

All review disciplines participated in labeling negotiations and review. Refer to CDTL review for summary of key labeling recommendations.

13. Postmarketing

- Postmarketing Risk Evaluation and Mitigation Strategies

  Routine pharmacovigilance

- Other Postmarketing Requirements and Commitments

  Existing accelerated approval PMRs 2060-2 and 3150-1 for NDA 205552 will carry over to this NDA. New PMR set numbers were issued for administrative purposes. Refer to action letter for final wording.

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.