CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217003Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	April 19, 2022
Application Type and Number:	NDA 217003
Product Name and Strength:	Imbruvica (ibrutinib) oral suspension, 70 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Pharmacyclics LLC (Pharmacyclics)
PNR ID #:	2022-1044724460
DMEPA 2 Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Imbruvica, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Pharmacyclics did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Imbruvica (ibrutinib) capsules were approved on November 13, 2013 under NDA 205552. Subsequently, Imbruvica tablets were approved on February 16, 2018 under NDA 210563. Imbruvica is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy; this indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Imbruvica is currently available as 70 mg and 140 mg oral capsules and 140 mg, 280 mg, 420 mg, and 560 mg oral tablets.

Pharmacyclics now submitted NDA 217003 ibrutinib oral suspension, 70 mg/mL, for the proposed indication for the treatment of pediatric patients with age 1 year and older with chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.

Thus, Pharmacyclics submitted the name, Imbruvica, for the newly proposed dosage formulation (i.e. oral suspension) for review under NDA 217003 on February 24, 2022.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 24, 2022 for Imbruvica (ibrutinib) oral suspension and the Prescribing Information for Imbruvica (ibrutinib) capsules and tablets.

Table 1. Relevant Product Information for Imbruvica (ibrutinib)

Product Name	**Imbruvica [proposed] (NDA 217003)**	**Imbruvica[a] (NDA 205552)**	**Imbruvica (NDA 210563)**
Initial Approval Date	Under Review	November 13, 2013	February 16, 2018
Intended Pronunciation	im-BRU-vih-kuh		
Active Ingredient	ibrutinib		
Indication	Imbruvica is a kinase inhibitor indicated for the treatment of adult patients with:		

[a] Calquence [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2019 NOV 21. Available from: https://www.accessdata fda.gov/drugsatfda_docs/label/2019/210259s006s007lbl.pdf

	• Mantle cell lymphoma (MCL) who have received at least one prior therapy. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. • Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) • Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion • Waldenström's macroglobulinemia (WM) • Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). *Imbruvica is indicated for the treatment of adult and pediatric patients age 1 year and older with:* *Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy. (proposed)*		
Route of Administration	Oral		
Dosage Form	*Oral Suspension*	Capsule	Tablet
Strength	70 mg/mL	(b) (4) mg	
Dose and Frequency	*Dose cGVHD:* • *Patients 12 years and older: 420 mg taken orally once daily* • *Patients 1 to < 12 years of age: 240 mg/m^2 taken orally once daily (up to a dose of 420 mg) (proposed)* • MCL and MZL: 560 mg taken orally once daily • CLL/SLL , and WM: 420 mg taken orally once daily		
How Supplied	*The Imbruvica (ibrutinib) oral suspension is a white to off-white suspension supplied as 108 mL in a 150 mL amber glass bottle with a pre-inserted bottle adapter and a child resistant closure. Each mL contains 70 mg of ibrutinib. The oral suspension bottle is provided in a carton with two 3 mL reusable oral*	The 70 mg capsules are supplied as yellow opaque capsules, marked with "ibr 70 mg" in black ink, in white HDPE bottles with a child-resistant closure: • 28 capsules per bottle The 140 mg capsules are supplied as white opaque capsules, marked with "ibr 140	The IMBRUVICA (ibrutinib) tablets are supplied in 4 strengths in the following packaging configurations: • 140 mg tablets: Yellow green to green round tablets debossed with "

	dosing syringes. (proposed)	mg" in black ink, in white HDPE bottles with a child-resistant closure: • 90 capsules per bottle • 120 capsules per bottle	ibr" on one side and "140" on the other side. Carton of one folded blister card containing two 14-count blister strips for a total of 28 tablets: NDC 57962-014-28 • 280 mg tablets: Purple oblong tablets debossed with " ibr" on one side and "280" on the other side. Carton of one folded blister card containing two 14-count blister strips for a total of 28 tablets: NDC 57962-280-28 • 420 mg tablets: Yellow green to green oblong tablets debossed with " ibr" on one side and "420" on the other side. Carton of one folded blister card containing two 14-count blister strips for a total of 28 tablets: NDC 57962-420-28

			• 560 mg tablets: Yellow to orange oblong tablets debossed with " ibr"on one side and "560" on the other side. Carton of one folded blister card containing two 14-count blister strips for a total of 28 tablets: NDC 57962-560-28
Storage	*Store the oral suspension bottle at 2°C to 25°C (36°F to 77°F). Do not freeze. (proposed)*	Store bottles at room temperature 20°C to 25°C (68°F to 77°F). Excursions are permitted between 15°C and 30°C (59°F to 86°F). Retain in original package until dispensing.	Store tablets in original packaging at room temperature 20°C to 25°C (68°F to 77°F). Excursions are permitted between 15°C and 30°C (59°F to 86°F).

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Imbruvica.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Imbruvica would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Imbruvica. The Division of Hematologic Malignancies 1 (DHM 1) did not comment on the findings of OPDP's assessment for Imbruvica.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Imbruvica.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[b].

2.2.2 Components of the Proposed Proprietary Name

Pharmacyclics did not provide a derivation or intended meaning for the proposed proprietary name, Imbruvica, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

The Division of Hematologic Malignancies 1 (DHM 1) did not forward any comments or concerns relating to Imbruvica at the initial phase of the review.

2.2.4 Evaluation of a Single Proprietary Name for Multiple Dosage Forms

We note that the newly proposed oral suspension formulation shares the same commercial ibrutinib drug substance that is used in the manufacture of the currently approved Imbruvica capsules (70 mg and 140 mg) and tablets (140 mg, 280 mg, 420 mg, and 560 mg) therefore, Pharmacyclics proposes to use Imbruvica as the proprietary name for ibrutinib oral suspension. Based on our understanding from the Prescribing Information at the time of this review, the proposed oral suspension dosage formulation is equivalent on a mg-per-mg basis with the currently approved Imbruvica formulations. It is a common and accepted practice to have a product line with multiple dosage forms managed under one proprietary name (e.g. Renvela and Pradaxa).

An oral suspension of ibrutinib was developed to allow once daily oral dosing for pediatric patients. Furthermore, we note that through our routine postmarket surveillance we have not identified any medication errors involving name confusion with the proprietary name Imbruvica. Therefore, given the precedence for using this naming convention, and the absence of any medication errors involving the proprietary name, we find Pharmacyclics proposal to market the proposed product with the proprietary name Imbruvica acceptable. The difference in the product characteristics between the three dosage formulations for Imbruvica may be managed through labels and labeling.

2.2.5 Communication of DMEPA's Determination

On April 19, 2022, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 1 (DHM 1).

3 CONCLUSION

The proposed proprietary name, Imbruvica, is acceptable.

[b] USAN stem search conducted on March 29, 2022.

If you have any questions or need clarifications, please contact Frances Fahnbulleh, OSE project manager, at 301-796-0942.

3.1 COMMENTS TO PHARMACYCLICS LLC

We have completed our review of the proposed proprietary name, Imbruvica, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on February 24, 2022, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [c]

[c] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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