CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210563Orig1s000
210563Orig2s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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Date of This Review:	12/19/2017
Application Type and Number:	NDA 210563
Product Name and Strength:	Imbruvica (ibrutinib) Tablets
Total Product Strength:	140 mg, 280 mg, 420 mg, and 560 mg
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Pharmacyclics, Inc.
Panorama #:	2017-17832328
DMEPA Safety Evaluator:	Casmir Ogbonna, PharmD, MBA, BCPS, BCGP
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director (Acting):	Mishale Mistry, PharmD, MPH

Contents

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 name are outlined in the reference section and Appendix A respectively. The Applicant did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Imbruvica (ibrutinib) was approved under NDA 205552 on November 13, 2013 as 140 mg capsules and is indicated for the treatment of mantle cell lymphoma (MCL) in patients who have received at least one prior therapy, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), CLL/SLL with 17p deletion, Waldenstrom's macroglobuminemia, marginal zone lymphoma who require systemic therapy and have received at least one prior anti-CD20-based therapy, and chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy. The Applicant proposes a tablet dosage form in strengths of 140 mg, 280 mg, 420 mg, and 560 mg, intended to be marketed for the treatment of the same approved indications as the currently approved capsule formulation. Thus, the Applicant submitted the name, Imbruvica, for the new dosage form under review for NDA 210563 on September 28, 2017.

1.2 PRODUCT INFORMATION

The following product information is provided in the September 28, 2017, proprietary name submission.

Table 1. Relevant Product Information for Imbruvica

Product	**Imbruvica (NDA 210563)**	**Imbruvica (NDA 205552)**
Initial Approval Date	Currently under review.	November 13, 2013
Active Ingredient	Ibrutinib	
Indication	Imbruvica is a Bruton's Tyrosine Kinase Inhibitor indicated for: • treatment of mantle cell lymphoma (MCL) in patients who have received at least one prior therapy • chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) • CLL/SLL with 17p deletion • Waldenstrom's macroglobuminemia (WM) • Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy • chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy	
Route of Administration	Oral	
Dosage Form:	Tablets	Capsules
Strength:	140 mg, 280 mg, 420 mg, 560 mg	140 mg

Dose and Frequency	MCL and MZL: 560 mg taken orally once daily CLL/SLL, WM, and cGVHD: 420 mg taken orally once daily	
How Supplied:	140 mg tablet: yellow green to green round tablets debossed with "ibr" on one side and "140" on the other side. 2 blisters of 14 count NDC 57962-014-28 280 mg tablet: purple oblong tablets debossed with "ibr" on one side and "280" on the other side. 2 blisters of 14 count NDC 57962-280-28 420 mg tablet: yellow green to green oblong tablets debossed with "ibr" on one side and "420" on the other side. 2 blisters of 14 count NDC 57962-420-28 560 mg tablet: yellow to orange oblong tablets debossed with "ibr" on one side and "560" on the other side. 2 blisters of 14 count NDC 57962-560-28	The white opaque 140 mg capsules marked with "ibr 140 mg" in black ink are available in white HDPE bottles with a child-resistant closure: • 90 capsules per bottle: NDC 57962-140-09 • 120 capsules per bottle: NDC 57962-140-12
Storage:	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.	

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Division of Hematology Products (DHP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed 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 are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 19, 2017 e-mail, the Division of Hematology Products (DHP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.4 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Imbruvica*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	November 14, 2017
Drug Name	Imbruvica [ibrutinib]
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED

[a] USAN stem search conducted on November 15, 2017.

Table 2. FAERS Search Strategy	
	INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	11/13/2013 to 11/14/2017 (FDA Receive Dates)

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

The search yielded 12 cases for review. After individual review, all 12 reports were not included in the final analysis for the following reasons: Inappropriate schedule (n = 6), drug dispensing error unrelated to Imbruvica (n = 1), drug dispensing error not related to Imbruvica (n = 1), drug dose omission (n = 2), drug administration error (n = 1), product storage error (n = 1).

Following exclusions, the search yielded no relevant cases related to name confusion with Imbruvica.

2.2.5 Multiple Dosage Forms under a Single Proprietary Name

Under NDA 210563, the Applicant proposes a tablet dosage form of Imbruvica, in strengths of 140 mg, 280 mg, 420 mg, and 560 mg to decrease patient pill burden. The Applicant proposes to market the new oral dosage form of tablets under the same proprietary name as the currently approved product, Imbruvica 140 mg capsules.

We note that the currently approved Imbruvica capsule dosage form shares the same active ingredient, indication, route of administration, dose, and frequency as the proposed tablet formulation. Additionally, we note that the two dosage forms will share a strength of 140 mg. Given the overlapping strength and the potential for the oral tablet and oral capsule to substituted for one another in practice, we consulted the DHP review team with regard to whether the dosage forms are equivalent on a mg per mg basis. Per the Office of Pharmaceutical Quality (OPQ) reviewer, the 140 mg tablets and 140 mg capsules differ solely on the inclusion of excipients, which are required for (b) (4) the tablets. The Applicant conducted dissolution tests, which demonstrate that the tablets and capsules are functionally equivalent. Per the clinical reviewer, the tablets and capsules can be substituted for one another with no clinical significance. Therefore, the risk of dosing errors due to converting between dosage forms is mitigated.

It is a common and accepted practice to have a product line with multiple dosage forms managed under one proprietary name within a single package insert. In this case, the residual risk of confusion between the capsule and tablet formulations of the product may be mitigated through labels and labeling intervention.

Moreover, we have not identified any relevant medication errors involving name confusion with the proprietary name Imbruvica. Therefore, we find the Applicant's proposal to market the proposed product with the proprietary name Imbruvica acceptable.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Hematology Products (DHP) via e-mail on December 18, 2017. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DHP on December 19, 2017, they stated no additional concerns with the proposed proprietary name, Imbruvica.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Neil Vora, OSE project manager, at 240-402-4845.

3.1 COMMENTS TO THE APPLICANT

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 September 28, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

2. ***Electronic Drug Registration and Listing System (eDRLS) database***

The electronic Drug Registration and Listing System (eDRLS) was established to supports the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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. [b]

[b] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

***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.

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

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/s/

CASMIR I OGBONNA
12/19/2017

MISHALE P MISTRY on behalf of HINA S MEHTA
12/19/2017

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