CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217729Orig1s000

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:	June 07, 2023
Application Type and Number:	NDA 217729
Product Name and Strength:	Bosulif (bosutinib) capsules, (b) (4), 50 mg and 100 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Pfizer, Inc. (Pfizer)
PNR ID #:	2023-1044725067
DMEPA 2 Safety Evaluator:	Sue Black, PharmD
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Bosulif, 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. Pfizer did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

On September 4, 2012, Bosulif (bosutinib) 100 mg and 500 mg tablets were approved under NDA 203341 for the treatment of adult patients with chronic, accelerated, or blast phase Ph+ chronic myelogenous leukemia (CML) with resistance, or intolerance to prior therapy. On October 27, 2017, the addition of a new 400 mg tablet strength was approved. On December 19, 2017, a new indication for the treatment of adult patients with newly diagnosed chronic phase (CP) Ph+ CML was approved.

Pfizer now proposes NDA 217729 for bosutinib capsules, (b) (4) 50 mg and 100 mg, for the proposed indication in adults and pediatric patients greater than or equal to 1 year of age with Newly diagnosed chronic phase Ph+ chronic myelogenous leukemia (CML) and chronic, (b) (4) Ph+CML with resistance or intolerance to prior therapy.

Thus, Pfizer submitted the name, Bosulif, for the newly proposed dosage formulation (i.e. capsule) for review under NDA 217729 on March 30, 2023.

On April 10, 2023, an information request was sent to Pfizer to clarify the strengths of the proposed product as the Request for Proprietary Name Review listed (b) (4) 50 mg and 100 mg, but the draft Prescribing Information listed only 50 mg and 100 mg. Subsequently, on April 12, 2023, Pfizer submitted an amendment to their request for proprietary name review[a] and stated the following:

> *"The proposed strengths for the bosutinib capsules included in the Request for Proprietary Name Review are* (b) (4) *50 mg, and 100 mg. The proposed capsule strengths for bosutinib in the draft United States Prescribing Information (USPI) are 50 mg and 100 mg. At the pre sNDA meeting held between the Agency and Pfizer on 11 October 2022, the Agency agreed to Pfizer's proposal to pursue a dose-banding approach supplemented by modeling and simulation to simplify the label for prescribers and pill burden for patients. If supported, this would enable inclusion of only the 50 mg and 100 mg capsule strengths in the USPI to support the final pediatric dose increment recommendations. The Agency has acknowledged Pfizer's proposal to include the* (b) (4)

[a] Bosutinib Formulation Response to 10 APR 2023 Information - Proprietary Name Review Request NDA 217729. San Diego (CA): Pfizer; 2023 APR 12. Available from: \\CDSESUB1\EVSPROD\nda217729\0003\m1\us\resp-ir-10apr2023-proprietary-name-review.pdf

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on March 30, 2023 and proposed Prescribing Information received on April 28, 2023 for Bosulif (bosutinib) capsules and the Prescribing Information for Bosulif (bosutinib) tablets.

Table 1. Relevant Product Information for Bosulif (bosutinib)		
Product Name	**Bosulif [proposed] (NDA 217729)**	**Bosulif [b] (NDA 203341)**
Initial Approval Date	Under Review	09/04/2012
Intended Pronunciation	BAH-suh-lif	
Active Ingredient	bosutinib	
Indication	Treatment of adults and pediatric patients greater than or equal to 1 year of age with: • Newly-diagnosed chronic phase Ph+ chronic myelogenous leukemia (CML) • Chronic, (b) (4) Ph+ CML with resistance or intolerance to prior therapy	Treatment of adults with: • Newly-diagnosed chronic phase Ph+ chronic myelogenous leukemia (CML) • Chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy
Route of Administration	Oral	
Dosage Form	capsules[c]	tablets
Strength	(b) (4) 50 mg, 100 mg	100 mg, 400 mg, 500 mg
Dose and Frequency	• Adults patients with newly-diagnosed chronic phase Ph+ CML: 400 mg orally once daily with food. • Adult patients with chronic, accelerated, or blast phase Ph+ CML	• Adults patients with newly-diagnosed chronic phase Ph+ CML: 400 mg orally once daily with food. • Adult patients with chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy:

[b] Bosulif [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2023 Apr 20. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/203341s024lbl.pdf.

[c] For patients who are unable to swallow an intact capsule(s), each capsule can be opened, and the content mixed with applesauce or yogurt.

	with resistance or intolerance to prior therapy: 500 mg orally once daily with food. • Pediatric patients with newly-diagnosed chronic phase Ph+ CML: 300 mg/m^2 orally once daily with food. • Pediatric patients with chronic, (b) (4) phase Ph+ CML with resistance or intolerance to prior therapy: 400 mg/m^2 orally once daily with food. • Consider dose escalation by increments of 100 mg once daily to a maximum of 600 mg daily in adult patients who do not reach complete hematologic, cytogenetic, or molecular response and do not have Grade 3 or greater adverse reactions. • Consider dose escalation by increments of 50 mg for those with a BSA <1.1 m^2 and 100 mg for those with a BSA >1.1 m^2 once daily to a maximum of 600 mg daily in pediatric patients who do not reach sufficient response after 3 months. • Adjust dosage for toxicity and organ impairment	500 mg orally once daily with food. • Consider dose escalation by increments of 100 mg once daily to a maximum of 600 mg daily in adult patients who do not reach complete hematologic, cytogenetic, or molecular response and do not have Grade 3 or greater adverse reactions. • Adjust dosage for toxicity and organ impairment
How Supplied	Capsules are supplied for oral administration in 2 strengths: 50 mg capsule: size 2 capsule, white body/orange cap with “BOS	Tablets are supplied for oral administration in 3 strengths: a 100 mg yellow, oval, biconvex, film-coated tablet debossed with “Pfizer” on one side and “100”

<table>
<tr><td></td><td>50” printed on the body and “Pfizer” printed on the cap in black ink. 100 mg capsule: size 0 capsule, white body/brownish-red cap with “BOS 100” printed on the body and “Pfizer” printed on the cap in black ink. Capsules are available in the following packaging configurations (Table 18).
BOSULIF Capsules
<table><tr><th>Package Configuration Count</th><th>Capsule Strength (mg)</th><th>NDC</th><th>Capsu</th></tr><tr><td>30 capsules per bottle</td><td>50</td><td>0069-0504-30</td><td>Size 2 capsule, with “BOS 50” “Pfizer” printed ink.</td></tr><tr><td>150 capsules per bottle</td><td>100</td><td>0069-1014-15</td><td>Size 0 capsule, red cap with “B body and “Pfize black ink.</td></tr></table></td><td>on the other; a 400 mg orange, oval, biconvex, film coated tablet debossed with “Pfizer” on one side and “400” on the other; and a 500 mg red, oval, biconvex, film-coated tablet debossed with “Pfizer” on one side and “500” on the other. Tablets are available in the following packaging configurations (Table 17):
BOSULIF Tablets
<table><tr><th>Package Configuration</th><th>Tablet Strength (mg)</th><th>NDC</th><th>Tablet Description</th></tr><tr><td>120 tablets per bottle</td><td>100 mg</td><td>0069-0135-01</td><td>Yellow, oval, biconvex, film tablets, debossed “Pfizer” on side and “100” on the other.</td></tr><tr><td>30 tablets per bottle</td><td>400 mg</td><td>0069-0193-01</td><td>Orange, oval, biconvex, film tablet debossed with “Pfizer” side and “400” on the other.</td></tr><tr><td>30 tablets per bottle</td><td>500 mg</td><td>0069-0136-01</td><td>Red, oval, biconvex, film-co tablets, debossed “Pfizer” on side and “500” on the other.</td></tr></table></td></tr>
<tr><td>Storage</td><td>Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) (b) (4)</td><td>Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].</td></tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Bosulif 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 Bosulif. The Division of Hematologic Malignancies 1 (DHM 1) concurred with the findings of OPDP’s assessment for Bosulif.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

[d] USAN stem search conducted on April 6, 2023.

2.2.2 Components of the Proposed Proprietary Name

Pfizer indicated in their submission that the proposed proprietary name, Bosulif, is an invented word with no inherent meaning and is derived from the prefix of the established name. The proposed name is comprised of a single word that contains the letters'-os-' which is the abbreviation for the 'left eye' route of administration. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of this abbreviation in the middle of the name, and the lack of prominence of this abbreviation makes it unlikely that the letters 'os' within the proposed proprietary name, Bosulif, could lead to confusion in this case. Beyond this abbreviation, we note that Bosulif that does not contain any additional components (i.e. a modifier, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On April 24, 2023, the Division of Hematologic Malignancies 1 (DHM 1) did not forward any comments or concerns relating to Bosulif 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 capsule formulation shares the same active ingredient as the currently approved Bosulif tablets. Based on the proposed Prescribing Information at the time of this review, the desired dose can be attained by combining different strengths of the proposed capsules and currently approved tablet formulation. In addition, the amount of bosutinib (active ingredient) in the respective tablets and capsule strengths is equivalent (e.g., the proposed 100 mg capsule is equivalent to the currently approved 100 mg tablet). 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). We also note both NDAs share the same PI.

The difference in the product characteristics (i.e., the dosage form, etc.) between the two dosage formulations for Bosulif may be managed through labels and labeling.

2.2.5 Communication of DMEPA's Determination

On June 7, 2023, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 1 (DHM 1).

3 CONCLUSION

The proposed proprietary name, Bosulif, is conditionally acceptable.

If you have any questions or need clarifications, please contact Candido Alicea, OSE project manager, at (240) 402-8310.

3.1 COMMENTS TO PFIZER, INC.

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

If any of the proposed product characteristics as stated in your submission, received on March 30, 2023 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.[e]

[e] 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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