

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

218785Orig1s000

218785Orig2s000

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:	November 25, 2024
Application Type and Number:	NDA 218785
Product Name, Dosage Form, and Strength:	Brukinsa (zanubrutinib) Tablet 160 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	BeiGene USA, Inc. (BeiGene)
PNR ID #:	2024-1044725967
DMEPA 2 Safety Evaluator:	Robbie Kattappuram, PharmD, BCPS
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1 INTRODUCTION

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

1.1 BACKGROUND AND REGULATORY HISTORY

Brukinsa (zanubrutinib) tablets, was approved on November 14, 2019 under NDA 213217 as a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. Brukinsa is currently marketed as an 80 mg capsule and additional indications have been approved (see Table 1).

BeiGene now proposes NDA 218785 zanubrutinib tablets, 160 mg, intended to be marketed for the treatment of the same approved indications as the currently approved capsules. (b) (4)

Thus, BeiGene submitted the name, Brukinsa, for the new dosage form under NDA 218785 on August 30, 2024.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 30, 2024^a for Brukinsa (zanubrutinib) tablets and the Prescribing Information for Brukinsa (zanubrutinib) capsules.

Table 1. Relevant Product Information for Brukinsa (zanubrutinib)		
Application Number	Brukinsa [proposed] (NDA 218785)	Brukinsa (NDA 213217)
Initial Approval Date	Under Review	November 14, 2019
Intended pronunciation:	broo kin' sah	
Active ingredient:	zanubrutinib	

^a Brukinsa (zanubrutinib) Prescribing Information. San Mateo (CA): BeiGene USA, Inc.; 2024 Jun. Available from: <\\CDSESUB1\EVSPROD\nda218785\0001\m1\us\brukinsa-zanu-tabs-oral-uspi-en-clean.docx>.

Table 1. Relevant Product Information for Brukinsa (zanubrutinib)		
Indication:	Treatment of adult patients with: • Mantle cell lymphoma (MCL) who have received at least one prior therapy • Waldenström's macroglobulinemia (WM) • Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti- CD20-based regimen. • Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). • Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.	
Dosage Form:	Tablet	Capsule
Strength:	160 mg	80 mg
Route of administration:	Oral	
Dose and frequency:	160 mg orally twice daily or 320 mg orally once daily	
How Supplied:	Bottle with a child-resistant cap containing 60 tablets. 160 mg, blue, oval, film-coated tablets debossed with "zanu" on one side and a functional score line on the other side	Bottle with a child-resistant cap containing 120 capsules. 80 mg, white to off-white opaque capsule, marked with "ZANU 80" in black ink
Storage:	(b) (4)	Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F)

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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

BeiGene did not provide a derivation or intended meaning for the proposed proprietary name, Brukinsa, in their submission. This proprietary name is comprised of a single word that contains the letters “in”, which is the abbreviation for the intranasal route of administration and the letters “ns”, which is the abbreviation for nasal spray route of administration, and “sa” indicating sustained action or an extended-release formulation. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of the letter strings, ‘in’ and ‘ns’ in the infix/suffix of the name are unlikely to be separated from the surrounding letters in a manner that would lead to confusion in this case. Thus, in this case, we do not object to the inclusion of the letters ‘in’ and ‘ns’.

As the letter string ‘sa’ is located at the end of the name, we evaluated the potential risk of misinterpreting the proposed proprietary name, Brukinsa, as “[drug name similar to Brukin] SA” and did not identify any concern.^c We note the letter string ‘sa’ is not listed on ISMP’s List of Error Prone Abbreviations, Symbols, or Dose Designations.^d Additionally, we note that the terminal letter string ‘sa’ is common in existing drug literature (e.g., Eucrisa, Rowasa, Sarclisa, etc.) and we are unaware of post-market reports of medication errors associated with this specific abbreviation through our routine surveillance. Thus, in this case, we do not object to the inclusion of the letters ‘sa’.

Beyond these abbreviations, we did not identify any other components (i.e., a modifier, dosage form, etc.) that can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

On October 8, 2024, the Division of Hematologic Malignancies 2 (DHM 2) did not forward any comments or concerns relating to Brukinsa 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 tablet formulation shares the same active ingredient, indications for use, frequency of administration, route of administration, and recommended dosing as the currently approved Brukinsa capsules. Our routine postmarket safety surveillance has not identified any medication error related proprietary name confusion with Brukinsa. BeiGene indicates the zanubrutinib tablet dosage form allows for improved ease of swallowing due to its reduced size and overall reduced tablet/capsule burden. Additionally, the functional scoring enables the tablet to be split to accommodate a reduced dose of 80 mg of zanubrutinib. Based on our understanding of the prescribing information and the assertion by Beigene that

^b USAN stem search conducted on September 4, 2024.

^c POCA search conducted on September 4, 2024 in version 5.9.

“clinical pharmacology evaluations support that the tablet exhibits bioequivalence with the capsule formulation” both the capsule and tablet are equivalent on a mg-per-mg basis at the time of this review. 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 prescribing information.

The difference in the product characteristics between the two dosage formulations for Brukinsa may be managed through labels and labeling.

2.2.5 COMMUNICATION OF DMEPA'S DETERMINATION

On November 25, 2024, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 2 (DHM 2).

3 CONCLUSION

The proposed proprietary name, Brukinsa, is conditionally acceptable.

3.1 COMMENTS TO BEIGENE USA, INC.

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

If any of the proposed product characteristics as stated in your submission, received on August 30, 2024 are altered prior to approval of the marketing application, the proprietary name must be resubmitted for review.

4 REFERENCES

1. *United States Adopted Names (USAN) Stems*

USAN Stems List contains all the recognized USAN stems, available at <https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-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 <https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms>).

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>).

Purple Book

The Purple Book is an online database that contains information about biological products, including biosimilar and interchangeable biological products, licensed (approved) by the FDA under the Public Health Service (PHS) Act. See Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, available at <https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or>.

Division of Medication Errors Prevention and Analysis pending proprietary name requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis.

5 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, the Office of Prescription Drug Promotion (OPDP) assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by the Office of Non-Prescription Drugs (ONPD). OPDP or ONPD 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 ONPD 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

*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.

^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 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.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, Cerner RxNorm, Purple Book, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score $\geq 70\%$.
- Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
- Low similarity: combined match percentage score $\leq 54\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
 - o Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in

the confusion of drug names^f. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.

- o Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
 - Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.
- c. FDA Prescription Simulation Studies: DMEPA also conducts prescription simulation studies using FDA health care professionals.

Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.
- d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND), Office of Generic Drugs (OGD), and/or Office of Pharmaceutical Quality (OPQ) for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-

^f Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the Safety Evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

Additionally, other review disciplines opinions such as OPQ may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary Safety Evaluator assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is $\geq$ 70%).			
Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).		
Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg	
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.	
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? • Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? • *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as z and f), is there a different number or	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$).

	placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	
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Table 5. Low Similarity Name Pair Checklist (i.e., combined score is $\leq 54\%$).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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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