CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761392Orig1s000
761392Orig2s000

PROPRIETARY NAME REVIEW(S)

SUFFIX REVIEW FOR NONPROPRIETARY NAME

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

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:	12/10/2024
Responsible OND Division:	select Division
Application Type and Number:	BLA 761392
Product Name and Strength:	Ospomyv (denosumab-dssb) injection, 60 mg/mL Xbryk (denosumab-dssb) injection, 120 mg/1.7 mL (70 mg/mL)
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung)
FDA Received Date:	February 12, 2024
Nexus NPNS ID #:	2024-234
DMEPA 2 Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 1 Director:	Mishale Mistry, PharmD, MPH

1 PURPOSE OF REVIEW

This review summarizes our evaluation of the four-letter suffixes proposed by Samsung for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761392.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On February 12, 2024, Samsung submitted a list of eight suffixes, in their order of preference, to be used in the nonproprietary name of their product[a]. Samsung also provided findings from their own evaluation of the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Samsung:

Table 1. Suffixes submitted by Samsung***

1.	dssb
2.	(b) (4)
3.	
4.	
5.	
6.	
7.	
8.	

We reviewed Samsung's proposed suffixes in the order of preference listed by Samsung, along with the supporting data they submitted, using the principles described in the applicable guidance.[b]

2.1 denosumab-dssb

Samsung's first proposed suffix, -dssb, is comprised of three distinct letters (d, s, b). We note that the letters 'ds' in the suffix represent the medical abbreviation for 'double strength'. We considered whether the

[a] Suffix Name Request BLA 761392. Incheon (Republic or Korea): Samsung Bioepis, Co., Ltd.; 2024 Feb 12. Available from: \\CDSESUB1\EVSPROD\bla761392\0001\m1\us\118-prop-names\suffix-name-request.pdf

[b] Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

inclusion of the letters ‘ds’ within the suffix could be misleading or a source of confusion and errors, but we could not identify a plausible risk based on the expected use of this product or based upon known causes of medication errors.

We determined that the proposed suffix -dssb, is not too similar to any other products’ suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA 1 ANALYSIS

These findings were shared with OPDP. On November 27, 2024, OPDP did not identify any concerns that would render this proposed suffix unacceptable. DMEPA 1 also communicated our findings to the select Division on December 10, 2024.

4 CONCLUSION

We find Samsung’s proposed suffix -dssb acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to denosumab-dssb. DMEPA 1 will communicate our findings to the Applicant via letter.

4.1 Recommendations for Samsung Bioepis Co., Ltd.

We find the nonproprietary name, denosumab-dssb, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, denosumab-dssb will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we will inform you of our findings.

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/

CARLOS M MENA-GRILLASCA
12/10/2024 11:53:46 AM

MISHALE P MISTRY
12/13/2024 02:35:28 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	October 22, 2024
Application Type and Number:	BLA 761392
Product Name, Dosage Form, and Strength:	Ospomyv (denosumab-xxxx)[a] injection, 60 mg/mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung Bioepis)
PNR ID #:	2024-1044725960
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP
DMEPA 1 Associate Director for Nomenclature and Labeling:	Idalia E. Rychlik, PharmD

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder denosumab-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

Table of Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Ospomyv, 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. Samsung Bioepis did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Samsung Bioepis previously submitted the proposed proprietary name, [(b) (4)]*** under BLA 761392 on February 12, 2024. However, on May 1, 2024, we found the name, [(b) (4)]*** unacceptable due to phonetic similarities and overlapping product characteristics with the pending proprietary name, [(b) (4)]***, and phonetic similarities and shared product characteristics with the proprietary name, [(b) (4)].[b]

Samsung Bioepis subsequently submitted the proposed proprietary name, [(b) (4)]*** under BLA 761392 on May 22, 2024. However, on July 25, 2024, we found the name unacceptable due to misbranding concerns.[c]

Thus, Samsung Bioepis submitted the proposed proprietary name, Ospomyv, for review on August 29, 2024 under BLA 761392.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 29, 2024[d] and the prescribing information received on September 10, 2024.[e]

Table 1. Relevant Product Information for Ospomyv	
Intended pronunciation:	Os'-poe-miv
Nonproprietary name:	denosumab-xxxx

[b] Bao, A. Proprietary Name Review for [(b) (4)]*** (BLA 761392). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 May 01. PNR ID No. 2024-1044725624.

[c] Bao, A. Proprietary Name Review for [(b) (4)]*** (BLA 761392). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 July 25. PNR ID No. 2024-1044725800.

[d] Proposed Proprietary Name [60 mg PFS] (Ospomyv BLA 761392). Incheon (Republic of Korea): Samsung Bioepis Co., Ltd.; 2024 Aug 29. Available from: \\CDSESUB1\evsprod\BLA761392\0022\m1\us\118-prop-names\proprietary-names-60mg.pdf

[e] Proposed prescribing information for Ospomyv. Incheon (Republic of Korea): Samsung Bioepis Co., Ltd.; 2024 Sep 10. Available from: \\CDSESUB1\evsprod\BLA761392\0024\m1\us\114-labeling\114a-draft-label\draft-labeling-60-mg-tracked.docx

Table 1. Relevant Product Information for Ospomyv	
Indication:	• Treatment of postmenopausal women with osteoporosis at high risk for fracture • Treatment to increase bone mass in men with osteoporosis at high risk for fracture • Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture • Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer • Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer
Dosage Form:	injection
Strength:	60 mg/mL
Route of administration:	Subcutaneous
Dose and frequency:	60 mg every 6 months
How Supplied:	Single-dose prefilled syringe with a safety guard
Storage:	Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton. Do not freeze. Prior to administration, product may be allowed to reach room temperature (up to 25°C/77°F) in the original container. Once removed from the refrigerator, product may be stored at room temperature for a single period of up to 60 days, but not exceeding the original expiry date. If not used within this period of up to 60 days, product may be returned to the refrigerator for 28 days for future use. Do not use after the expiry date printed on the label. Protect from direct light and heat. Avoid vigorous shaking.
Reference Product:	Ospomyv (denosumab-xxxx) is a proposed interchangeable to US-licensed Reference Product, Prolia (denosumab) BLA 125320

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Samsung Bioepis indicated in their submission that the proposed proprietary name, Ospomyv, is derived from the words "osteoporosis" and "movement". This proprietary name is comprised of a single word that contains the medical abbreviations for "left eye" (i.e., "OS") and "by mouth" (i.e., "PO") within the name. Although we typically discourage the incorporation of medical abbreviations in proprietary names, we evaluated the potential risk of misinterpreting the proposed proprietary name Ospomyv as "OS [drug name similar to Pomyv]". A POCA search of the name "Pomyv" did not identify any names that would pose a risk for confusion.[g] Additionally, we determined that the location of the letter string "-po-" within the proposed proprietary name is unlikely to be separated from the surrounding letters in a manner that could lead to a medication error.

Thus, we conclude that the abbreviations "os" and "po" in the name are acceptable. Beyond these abbreviations, we note that Ospomyv does not contain any additional 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

On October 2, 2024, the Division of General Endocrinology (DGE) did not forward any comments or concerns relating to Ospomyv at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Eighty-six (86) practitioners participated in DMEPA's prescription simulation studies for Ospomyv. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search[h] identified 12 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 2 below.

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[f] USAN stem search conducted on September 13, 2024.

[g] POCA search conducted on September 13, 2024 in version 5.9.

[h] POCA search conducted on September 13, 2024 in version 5.9.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

Table 2. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	11
Low similarity name pair: combined match percentage score ≤54%	0

2.2.7 SAFETY ANALYSIS OF NAMES WITH POTENTIAL ORTHOGRAPHIC, SPELLING, AND PHONETIC SIMILARITIES

Our analysis of the 12 names contained in Table 2 determined none of the names will pose a risk for confusion with Ospomyv as described in Appendices C through H.

2.2.8 DISCUSSION OF DUAL PROPRIETARY NAME

Samsung Bioepis intends to market denosumab-xxxx under two different proprietary names: Ospomyv (BLA 761392) and Xbryk*** (BLA 761392). Table 3 compares the two proposed proprietary names and their respective product characteristics.

Table 3. Relevant Product Information for Ospomyv and Xbryk***		
Product Name	Ospomyv	Xbryk***
Intended Pronunciation	Os'-poe-miv	Ex'-brik
Nonproprietary Name	denosumab-xxxx	
Indication	Treatment of postmenopausal women with osteoporosis at high risk for fracture. Treatment to increase bone mass in men with osteoporosis at high risk for fracture Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture Treatment to increase bone mass in men at high risk for fracture receiving androgen	Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Table 3. Relevant Product Information for Ospomyv and Xbryk***		
Product Name	Ospomyv	Xbryk***
	deprivation therapy for nonmetastatic prostate cancer Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer	Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.
Route of Administration	subcutaneous	
Dosage Form	injection	
Strength	60 mg/mL	120 mg/1.7 mL (70 mg/mL)
Dose and Frequency	60 mg subcutaneous injection once every 6 months	Multiple Myeloma and Bone Metastasis from Solid Tumors: 120 mg administered as a subcutaneous injection every 4 weeks. Giant Cell Tumor of Bone: 120 mg administered every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Hypercalcemia of Malignancy: 120 mg administered every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.
How Supplied	Single-dose prefilled syringe, 1 (b) (4) per carton	120 mg/1.7 mL single-dose vial, 1 vial per carton
Reference Product	Proposed interchangeable biosimilar to US-licensed Reference Product, Prolia (denosumab) BLA 125320	Proposed interchangeable biosimilar to US-licensed Reference Product, Xgeva (denosumab) BLA 125320

Appears this way on original

de a rationale of the proposal to use a dual proprietary name for this
that US-licensed Reference Products, Prolia and Xgeva (BLA 125320), also use a dual proprietary naming strategy.

We have evaluated the risks associated with the proposed dual proprietary name strategy and do not object to the use of a dual proprietary name in this case.

2.2.9 COMMUNICATION OF DMEPA'S DETERMINATION

On October 22, 2024, DMEPA 1 communicated our determination to the Division of General Endocrinology (DGE).

3 CONCLUSION

The proposed proprietary name, Ospomyv, is conditionally acceptable.

3.1 COMMENTS TO SAMSUNG BIOEPIS CO., LTD.

We have completed our review of the proposed proprietary name, Ospomyv, 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 29, 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 3*. 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.[i]

*Table 3. 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.

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

*Table 3. 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 ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 4-6) 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 4).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - 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[j]. 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.

- 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 5).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) 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-

[j] 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 4. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 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? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	Y/N	Do the names have different number of syllables?
Y/N	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.*	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>
<tr><th colspan="3">Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).</th></tr>
<tr><td>Step 1</td><td colspan="2">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</td></tr>
<tr><td>Step 2</td><td colspan="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.</td></tr>
<tr><td></td><td>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</td><td>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?</td></tr>
</table>

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤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?	

Table 6. Low Similarity Name Pair Checklist (i.e., combined score is **≤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.

APPENDIX B. PRESCRIPTION SIMULATION SAMPLES AND RESULTS

Figure 1. Ospomyv Study (Conducted on 9/6/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order: Ospomyv Inject 60mg subcutaneously today Outpatient Prescription: Ospomyv Inject 60 mg subcut once every 6 months #1 prefilled syringe Dr. _____ Address	Ospomyv Inject 60 mg subcutaneously once every 6 months #1 prefilled syringe
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Ospomyv	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Ospomyv People Received Study: 190 People Responded: 86					
Total	20	23	21	22	86
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
ASPOMIS	0	0	1	0	1
ASPOMIV	0	0	3	0	3
AZPOMEV	0	0	2	0	2
AZPOMIV	0	0	1	0	1
OSPANYR	1	0	0	0	1
OSPMYV	1	0	0	0	1
OSPOMIV	0	0	3	0	3
OSPOMYR	2	0	0	0	2
OSPOMYU	0	2	0	0	2
OSPOMYV	14	20	0	22	56
OSPONUYV	1	0	0	0	1
OSPOYV	0	1	0	0	1
OZMPOMIV	0	0	1	0	1
OZPOMEV	0	0	1	0	1
OZPOMIV	0	0	7	0	7
OZPOMYV	1	0	0	0	1
OZPULMIV	0	0	1	0	1

ZPOMIV	0	0	1	0	1

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is **≥70%)**

No.	Proposed name: Ospomyv Pronunciation: Os'-poe-miv Established name: denosumab-xxxx Dosage form: injection Strength(s): 60 mg/mL Dosage: 60 mg subcutaneously every 6 months	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Ospomyv	100	This name is the subject of this review.

APPENDIX D. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Opsynvi	60

APPENDIX E. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Ospomyv Pronunciation: Os'-poe-miv Established name: denosumab-xxxx Dosage form: injection Strength(s): 60 mg/mL Dosage: 60 mg subcutaneously every 6 months	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	Optimis7	62	This name pair has sufficient orthographic and phonetic differences.
2.	Opsumit	60	This name pair has sufficient orthographic and phonetic differences.

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is **≤54%)** – N/A

APPENDIX G. Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Optimyd	68	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
2.	Optomycin	58	Brand discontinued with no generic equivalents available. ANDA 062171 withdrawn FR effective 04/26/1996.
3.	Osmovist 190	58	Brand discontinued with no generic equivalents available. NDA 019580 withdrawn FR effective 06/10/1999.
4.	Osmovist 240	58	Brand discontinued with no generic equivalents available. NDA 019580 withdrawn FR effective 06/10/1999.
5.	(b) (4) ***	56	Proposed proprietary name for IND (b) (4) found to be acceptable (OSE # (b) (4)), however, the entire application was withdrawn by the Applicant on (b) (4).

APPENDIX H. Names not likely to be confused due to absence of attributes that are known to cause name confusion[k].

No.	Name	POCA Score (%)
1.	Ascomp	60
2.	Stomax	56
3.	Osmoglyn	55

[k] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

AMY J BAO
10/22/2024 11:11:11 AM

YEVGENIYA M KOGAN
10/22/2024 02:52:35 PM

IDALIA E RYCHLIK
10/22/2024 02:54:14 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	July 25, 2024
Application Type and Number:	BLA 761392
Product Name, Dosage Form, and Strength:	(b) (4) (denosumab-xxxx)[a] injection, 60 mg/mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung Bioepis)
PNR ID #:	2024-1044725800
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP
DMEPA 1 Associate Director for Nomenclature and Labeling:	Idalia E. Rychlik, PharmD

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[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder denosumab-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

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/s/

AMY J BAO
07/25/2024 11:29:21 AM

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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	May 1, 2024
Application Type and Number:	BLA 761392
Product Name, Dosage Form, and Strength:	(b) (4) (denosumab-xxxx)[a] injection, 60 mg/mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung Bioepis)
PNR ID #:	2024-1044725624
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP
DMEPA 1 Associate Director for Nomenclature & Labeling:	Idalia E. Rychlik, PharmD

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[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder denosumab-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

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05/01/2024 01:32:17 PM

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05/01/2024 03:09:25 PM

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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 12, 2024
Application Type and Number:	BLA 761392
Product Name, Dosage Form, and Strength:	Xbryk (denosumab-xxxx)[a] injection, 120 mg/1.7 mL (70 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung Bioepis)
PNR ID #:	2024-1044725625
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP
DMEPA 1 Associate Director for Nomenclature & Labeling:	Idalia E. Rychlik, PharmD

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder denosumab-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

Table of Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Xbryk, 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. Samsung Bioepis did not submit an external name study for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 12, 2024[b] and the prescribing information received on February 12, 2024.[c]

Table 1. Relevant Product Information for Xbryk	
Intended pronunciation:	Ex'-brik
Nonproprietary name:	denosumab-xxxx
Indication:	• Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. • Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. • Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.
Dosage Form:	injection
Strength:	120 mg/1.7 mL (70 mg/mL)
Route of administration:	subcutaneous
Dose and frequency:	Multiple myeloma and bone metastasis from solid tumors: • 120 mg every 4 weeks Giant cell tumor of bone: • 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy Hypercalcemia of malignancy: • 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy
How Supplied:	Single-dose vial

[b] Proposed Proprietary Name [120 mg Vial] (Xbryk BLA 761392). Incheon (Korea): Samsung Bioepis Co., Ltd.; 2024 FEB 12. Available from: \\CDSESUB1\evsprod\BLA761392\0001\m1\us\118-prop-names\proprietary-names-120mg.pdf

[c] Proposed prescribing information for Xbryk. Incheon (Korea): Samsung Bioepis Co., Ltd.; 2024 FEB 12. Available from: \\CDSESUB1\EVSPROD\bla761392\0001\m1\us\114-labeling\114a-draft-label\draft-labeling-120mg-clean.docx

Table 1. Relevant Product Information for Xbryk	
Storage:	Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton. Do not freeze. Once removed from the refrigerator, product may be stored at room temperature for a single period of up to 60 days, but not exceeding the original expiry date. If not used within this period of up to 60 days, product may be returned to the refrigerator for future use. Do not use after the expiry date printed on the label. Protect from direct light and heat. Avoid vigorous shaking.
Reference Product:	Xbryk (denosumab-xxxx) is a proposed interchangeable to US-licensed Reference Product, Xgeva (denosumab) BLA 125320

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

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

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

Samsung Bioepis indicated in their submission that the proposed proprietary name, Xbryk, is derived from the concept that the proposed medicinal product prevents ("X") bone "breakage". 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

On March 14, 2024, the Division of General Endocrinology (DGE) did not forward any comments or concerns relating to Xbryk at the initial phase of the review.

[d] USAN stem search conducted on April 1, 2024.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Seventy-eight (78) practitioners participated in DMEPA's prescription simulation studies for Xbryk. We removed one response, [redacted]***, as the respondent entered multiple responses in error likely due to having multiple studies open at one time. The remaining responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

Appendix B contains 77 results from the prescription simulation studies.

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search[e] identified three names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 2 below.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

Table 2. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	2
Low similarity name pair: combined match percentage score ≤54%	0

2.2.7 SAFETY ANALYSIS OF NAMES WITH POTENTIAL ORTHOGRAPHIC, SPELLING, AND PHONETIC SIMILARITIES

Our analysis of the three names contained in Table 2 determined none of the names will pose a risk for confusion with Xbryk as described in Appendices C through H.

2.2.8 DISCUSSION OF DUAL PROPRIETARY NAME

Samsung Bioepis intends to market denosumab-xxxx under two different proprietary names: [redacted]*** (BLA 761392) and Xbryk (BLA 761392). Table 3 compares the two proposed proprietary names and their respective product characteristics.

Table 3. Relevant Product Information for [redacted]*** and Xbryk		
Product Name	[redacted]***	**Xbryk**
Initial Approval Date	N/A	N/A

[e] POCA search conducted on April 1, 2024 in version 5.7.

Table 3. Relevant Product Information for [redacted]*** and Xbryk		
Product Name	[redacted]***	**Xbryk**
Intended Pronunciation	[redacted]	Ex'-brik
Nonproprietary Name	denosumab-xxxx	
Indication	Treatment of postmenopausal women with osteoporosis at high risk for fracture. Treatment to increase bone mass in men with osteoporosis at high risk for fracture Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer	Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.
Route of Administration	subcutaneous	
Dosage Form	injection	
Strength	60 mg/mL	120 mg/1.7 mL (70 mg/mL)
Dose and Frequency	60 mg subcutaneous injection once every 6 months	<u>Multiple Myeloma and Bone Metastasis from Solid Tumors</u>: 120 mg administered as a subcutaneous injection every 4 weeks. <u>Giant Cell Tumor of Bone</u>: 120 mg administered every 4 weeks with additional 120 mg

Table 3. Relevant Product Information for [redacted]*** and Xbryk		
Product Name	[redacted]***	**Xbryk**
		doses on Days 8 and 15 of the first month of therapy. Hypercalcemia of Malignancy: 120 mg administered every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy.
How Supplied	Single-dose prefilled syringe, 1 [redacted] per carton	120 mg/1.7 mL single-dose vial, 1 vial per carton
Reference Product	Proposed interchangeable biosimilar to US-licensed Reference Product, Prolia (denosumab) BLA 125320	Proposed interchangeable biosimilar to US-licensed Reference Product, Xgeva (denosumab) BLA 125320

Although both products contain the same active ingredients, they have different indications, strengths, dosages, and are supplied in different presentations (see Table 3). We note that the Applicant did not provide a discussion of the proposal to use a dual proprietary name for this product. However, we note that US-licensed Reference Products (Prolia (denosumab) injection and Xgeva (denosumab) injection) also use a dual proprietary naming strategy.

We evaluated the risks associated with this naming strategy and note that there is a potential for concomitant therapy since postmarketing experience with other drug products has shown concomitant therapy to be a common type of error when an active ingredient is marketed under two or more names.[f] However, given these products will have different indications, strengths, dosages, and presentations, managing them under separate names may decrease the likelihood of confusion. Therefore, we do not object to the use of a dual proprietary name in this case. Any residual risk may be managed through labels and labeling mitigations.

2.2.9 COMMUNICATION OF DMEPA'S DETERMINATION

On April 12, 2024, DMEPA 1 communicated our determination to the Division of General Endocrinology (DGE).

3 CONCLUSION

The proposed proprietary name, Xbryk, is conditionally acceptable.

If you have any questions or need clarifications, please contact Deveonne Hamilton-Stokes, OSE project manager, at 301-796-2253.

[f] The Institute for Safe Medication Practices. "Revatio=Sildenafil=Viagra". January 2009

3.1 COMMENTS TO SAMSUNG BIOEPIS CO., LTD.

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

If any of the proposed product characteristics as stated in your submission, received on February 12, 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 3*. 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.[g]

*Table 4. 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.

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

*Table 4. 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 ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 4-6) 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 4).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - 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[h]. 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.

- 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 5).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) 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.

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

Additionally, when applicable, at the same time DMEPA requests concurrence/non-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 5. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 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? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	Y/N	Do the names have different number of syllables?
Y/N	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.*	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 6: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤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	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 6: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤69%).**		
	there a different number or 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?	

Table 7. Low Similarity Name Pair Checklist (i.e., combined score is **≤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.

APPENDIX B. PRESCRIPTION SIMULATION SAMPLES AND RESULTS

Figure 1. Xbryk Study (Conducted on 2/16/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order: Xbryk Inject 120 mg subcutaneously today Xbryk Inject 120 mg subcutaneously once every 4 weeks # 1 vial Outpatient Prescription:	Xbryk Inject 120 mg subcutaneously once every 4 weeks Dispense 1 vial
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Xbryk	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Xbryk People Received Study: 164 People Responded: 77					
Total	20	20	19	18	77
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
AXBRIC	0	0	1	0	1
AXBRICK	0	0	1	0	1
AXBRIK	0	0	1	0	1
EXBREK	0	0	1	0	1
EXBREQ	0	0	1	0	1
EXBRIC	0	0	1	0	1
EXBRICK	0	0	6	0	6
EXBRIK	0	0	1	0	1
EXBRIQ	0	0	4	0	4
IBRYK	0	1	0	0	1
KBRYK	3	0	0	0	3
XBREYK	1	0	0	0	1
X-BRICK	0	0	1	0	1
XBRIK	1	0	0	0	1
XBRIX	0	0	1	0	1
XBRYK	14	18	0	18	50
XBRZK	1	0	0	0	1

XFRYK	0	1	0	0	1

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is **≥70%)**

No.	Proposed name: Xbryk Pronunciation: Ex'-brik Established name: denosumab-xxxx Dosage form: injection Strength(s): 120 mg/1.7 mL (70 mg/mL) Dosage: 120 mg every 4 weeks	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	Xbryk	100	This name is the subject of this review.

APPENDIX D. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	X-Prep	59

APPENDIX E. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Xbryk Pronunciation: Ex'-brik Established name: denosumab-xxxx Dosage form: injection Strength(s): 120 mg/1.7 mL (70 mg/mL) Dosage: 120 mg every 4 weeks	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	Adbry	59	This name pair has sufficient orthographic and phonetic differences.

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is **≤54%)** – N/A

APPENDIX G. Names not likely to be confused or not used in usual practice settings for the reasons described. – N/A

APPENDIX H. Names not likely to be confused due to absence of attributes that are known to cause name confusion[i]. – N/A

[i] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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