

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215400Orig1s000

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:	February 7, 2025
Application Type and Number:	NDA 215400
Product Name, Dosage Form, and Strength:	Brekiya (dihydroergotamine mesylate) injection 1 mg/mL
Product Type:	Combination Product (Drug-Device): Autoinjector
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Amneal Pharmaceuticals LLC (Amneal)
PNR ID #:	2024-1044726108
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

Sun Pharma (former owner of NDA 215400) previously submitted the proposed proprietary name Brekiya on June 24, 2021. However, we found the name unacceptable due to orthographic similarities and overlapping product characteristics with another pending proprietary name, (b) (4) *** under NDA 215400 on September 21, 2021.^a Therefore, the ultimate acceptability of the proposed proprietary name, Brekiya, was dependent upon which underlying application was approved first.

Subsequently, Sun Pharma submitted the name, (b) (4) *** for review on October 14, 2021. However, Sun Pharma withdrew the name (b) (4) *** on December 10, 2021^b because the proposed name, Brekiya remained their preferred proposed proprietary name for this product. We also note that the other affected application holder of the conflicting name (b) (4) *** submitted an alternative name, (b) (4) *** for review on November 2, 2021, which was found conditionally acceptable on May 16, 2022.^c

On December 10, 2021, the Sun Pharma resubmitted their preferred proprietary name, Brekiya for review under NDA 215400. At the time of our review, we noted that the goal date for NDA 215400 was January 19, 2022, whereas the underlying application for (b) (4) *** remained in IND status. Therefore, we determined NDA 215400 approval will precede approval of the application with the conflicting proposed name (b) (4) ***. As such, we found the proposed name, Brekiya conditionally acceptable under NDA 215400 on December 21, 2021.^d However, NDA 215400 received a complete response (CR) letter on January 18, 2022, due to product quality and facility inspection issues.

On April 6, 2022, the rights, title, and ownership of NDA 215400 were transferred from Sun Pharmaceutical Industries Limited (Sun Pharma) to Amneal Pharmaceuticals LLC (Amneal).

Thus, Amneal resubmitted the name, Brekiya for review on January 18, 2023, as part of the Class 2 Resubmission for NDA 215400. At the time of our review, we noted that the new goal date for NDA 215400 was July 18, 2023, whereas the underlying application for (b) (4) ***

^a Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 SEP 21. PNR ID No. 2021-1044724038.

^b Withdrawal of Proprietary name for (b) (4) *** (NDA 215400) available from docuBridge via:
<\\CDSESUB1\evsprod\nda215400\0023\m1\us\cover-letter-pnr-withd.pdf>

^c Birkemeier D. Proprietary Name Review for (b) (4) *** (IND (b) (4)). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 MAY 16. PNR ID No. 2021-1044724266.

^d Weitzman, B. Proprietary Name Memorandum for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 DEC 21. PNR ID No. 2021-1044724326.

(b) (4) Therefore, we determined NDA 215400 approval will precede approval of the application with the conflicting proposed name (b) (4) ***. As such, we found the proposed name, Brekiya conditionally acceptable under NDA 215400 on April 6, 2023.^e However, NDA 215400 received a second complete response (CR) letter on July 18, 2023, due to facility inspection issues.

Thus, Amneal resubmitted the name Brekiya for review on November 15, 2024, as part of the Class 2 Resubmission for NDA 215400.

We note that the new goal date for NDA 215400 is May 15, 2025, whereas the underlying application for (b) (4) *** (b) (4) Therefore, if the proposed proprietary name, Brekiya, is granted approval under NDA 215400 on or before May 15, 2025, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) ***.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 15, 2024^f

Table 1. Relevant Product Information for Brekiya	
Intended pronunciation:	breh kee' yah
Active ingredient:	dihydroergotamine mesylate
Indication:	For the acute treatment of migraine headaches with or without aura and the acute treatment of cluster headache episodes.
Dosage Form:	Injection (autoinjector)
Strength:	1 mg/mL
Route of administration:	subcutaneous
Dose and frequency:	1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.
How Supplied:	Available as a clear, colorless, sterile solution in 1 mL prefilled syringe assembled in a single dose autoinjector containing 1 mg of dihydroergotamine mesylate per mL, in a carton pack.
Storage:	Store at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Do not refrigerate or freeze. Protect from light. Retain in original pack until time of use.

^e Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 APR 6. PNR ID No. 2023-1044724950.

^f Proprietary name Request for Brekiya (NDA 215400). Brookhaven (NY): Amneal Pharmaceuticals LLC; 2024 DEC 10. Available from: <\\CDSESUB1\EVSPROD\nda215400\0038\m1\us\1-18-proprietary-names.pdf>

Table 1. Relevant Product Information for Brekiya	
Reference Listed Drug:	D.H.E. 45 (dihydroergotamine mesylate) NDA 005929

2 DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Brekiya would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Brekiya. However, the Division of Neurology 2 (DN 2) did not provide comment regarding OPDP's assessment.

2.2 SAFETY ASSESSMENT

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

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

There is no USAN stem present in the proposed proprietary name.^g

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

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

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

The Division of Neurology 2 (DN 2) did not forward any comments or concerns relating to Brekiya at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

Ninety-four practitioners participated in DMEPA's prescription simulation studies for Brekiya.

Three respondents in the voice study misinterpreted the proposed proprietary name as "Reqia" [n=1] and "Requia" [n=2] which are close variations of the currently marketed product, Requip. We previously evaluated the name pair, Brekiya and Requip, under NDA 215400 (OSE# 2021-1044724038 dated September 21, 2021) and determined that there are sufficient orthographic, phonetic, and product characteristic differences between the name pair. Thus, we maintain our previous decision that the risk of name confusion between this name pair is minimized.

^g USAN stem search conducted on January 12, 2025.

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 the results from the prescription simulation studies.

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search^h identified 56 names with a combined score of $\geq 55\%$ or an individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed, and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 7 names not previously analyzed. 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 $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	5
Low similarity name pair: combined match percentage score $\leq 54\%$	2

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

Our analysis of the 7 names contained in Table 2 determined none of the names will pose a risk for confusion with Brekiya as described in Appendices C through H.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On February 7, 2025, DMEPA 2 communicated our determination to the Division of Neurology 2 (DN 2).

3 CONCLUSION

The proposed proprietary name, Brekiya, is conditionally acceptable.

^h POCA search conducted on January 12, 2025 in version 5.9.

3.1 COMMENTS TO AMNEAL PHARMACEUTICALS LLC

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

If any of the proposed product characteristics as stated in your submission, received on November 15, 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 $\geq 70\%$.
- 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 (Tables 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 that 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.
 - 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^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.

- 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 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 and 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, Chan, I, and Taylor, K. 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 $\geq$ 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 as 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 5: 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 as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: 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 names appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	
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Table 6. 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.

APPENDIX B. PRESCRIPTION SIMULATION SAMPLES AND RESULTS

Figure 1. Brekiya Study (Conducted on 11/29/2024)

Handwritten Medication Order Prescription	Verbal Prescription
<u>Medication Order:</u> <i>Brekiya Inject 1mg SQ PRN</i>	Brekiya Inject 1 mg subcutaneously as needed Dispense #1
<u>Outpatient Prescription:</u> Patient _____ Date <u>11-29-24</u> Address _____ Rx <i>Brekiya</i> <i>Inject 1mg subcutaneously as needed</i> <i>#1</i> Refill(s): _____ Dr. <u>SE</u> DEA No. _____ Address _____ Telephone _____	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Brekiya	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Brekiya					
People Received Study: 180					
People Responded: 94					
Total	27	27	16	24	94
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
BRABIYA	0	1	0	0	1
BRAKIYA	0	1	0	0	1
BRAKYA	0	0	1	0	1
BREBIGA	0	1	0	0	1
BREBIGE	0	1	0	0	1
BREBIYA	0	8	0	0	8
BRECKIA	0	0	1	0	1
BREFEIYA	1	0	0	0	1

BREKEYA	0	0	1	0	1
BREKIA	0	0	4	0	4
BREKIYA	26	15	0	24	65
BREKKIA	0	0	1	0	1
BREKYA	0	0	1	0	1
BREQIA	0	0	1	0	1
BREQUIA	0	0	2	0	2
RAKEYA	0	0	1	0	1
REQIA	0	0	1	0	1
REQUIA	0	0	2	0	2

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is $\geq 70\%$)

No.	Proposed name: Brekiya Pronunciation: breh kee' yah Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Dosage: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.
	N/A		

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

No.	Name	POCA Score (%)
	N/A	

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

No.	Proposed name: Brekiya Pronunciation: breh kee' yah Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Dosage: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.	(b) (4) ***	56	This name pair has sufficient orthographic and phonetic differences.
2.	(b) (4) ***	55	This name pair has sufficient orthographic and phonetic differences.

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
1.	Beizray	48

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.	(b) (4) ***	59	Proposed proprietary name for IND (b) (4) found unacceptable by DMEPA due to misbranding concerns (b) (4) is active, and no new names have been submitted.
2.	(b) (4) ***	54	Proposed proprietary name for NDA 216665 found unacceptable by DMEPA due to a conflict with a marketed product (OSE# 2024-1044725865 dated September 24, 2024). Subsequently, the proposed proprietary name, Vykath*** was found conditionally acceptable for NDA 216665 (OSE# 2024-1044726024 dated November 22, 2024).

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.	(b) (4) ***	62
2.	Mresvia	60

^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

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/

BEVERLY WEITZMAN
02/07/2025 09:20:09 AM

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02/07/2025 11:28:05 AM

HINA S MEHTA
02/07/2025 02:04:38 PM

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	April 6, 2023
Application Type and Number:	NDA 215400
Product Name and Strength:	Brekiya (dihydroergotamine mesylate) injection (autoinjector), 1 mg/mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Amneal Pharmaceuticals LLC (Amneal)
PNR ID #:	2023-1044724950
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Acting Team Leader:	Stephanie DeGraw, PharmD
DMEPA 2 Director:	Danielle Harris, PharmD

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1 INTRODUCTION

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

1.1 REGULATORY HISTORY

(b) (4) (former owner of NDA 215400) previously submitted the proposed name Brekiya on June 24, 2021. However, we found the name unacceptable due to orthographic similarities and shared product characteristics with another pending proprietary name, (b) (4) *** under NDA 215400 on September 21, 2021.^a Therefore, the ultimate acceptability of the proposed proprietary name, Brekiya, was dependent upon which underlying application was approved first.

Subsequently, (b) (4) submitted the name, (b) (4) *** for review on October 14, 2021. However, (b) (4) withdrew the name (b) (4) *** on December 10, 2021^b because the proposed name, Brekiya remained their preferred proposed proprietary name for this product. We also note that the other affected application holder of the conflicting name (b) (4) *** submitted an alternative name, (b) (4) *** for review on November 2, 2021, which was found acceptable on May 16, 2022.^c

On December 10, 2021, the (b) (4) resubmitted their preferred proprietary name, Brekiya for review. At the time of our review, we note that the goal date for NDA 215400 was January 19, 2022, whereas the underlying application for (b) (4) ** (b) (4). Therefore, we determined NDA 215400 approval will precede approval of the application with the conflicting proposed name (b) (4) ***. As such, we found the proposed name, Brekiya conditionally acceptable under NDA 215400 on December 21, 2021.^d However, NDA 215400 received a complete response (CR) letter on January 18, 2022.

On April 6, 2022, the rights, title, and ownership of NDA 215400 were transferred from Sun Pharmaceutical Industries Limited (Sun Pharma) to Amneal Pharmaceuticals LLC (Amneal).^e

On January 18, 2023, Amneal submitted a Class 2 Resubmission to NDA 215400 to address the deficiencies identified in the CR letter.

^a Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 SEP 21. Panorama No. 2021-1044724038.

^b Withdrawal of Proprietary name for (b) (4) *** (NDA 215400) available from docuBridge via: <\\CDSESUB1\evsprod\nda215400\0023\m1\us\cover-letter-pnr-withd.pdf>

^c Birkemeier D. Proprietary Name Review for (b) (4) ** (IND (b) (4)). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); (b) (4).

^d Weitzman, B. Proprietary Name Review for (b) (4) (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 DEC 21. Panorama No. 2021-1044724326.

^e Administration/Transfer of Applicant proposed under NDA 215400 available from: <\\CDSESUB1\EVSPROD\nda215400\0025\m1\us\1-2-cover-letter-seq-0025-20220406.pdf>

We note that the new goal date for NDA 215400 is July 18, 2023, whereas the underlying application for (b) (4) *** (b) (4) Therefore, if the proposed proprietary name, Brekiya, is granted approval under NDA 215400 on or before July 18, 2023, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) ***.

Thus, Amneal resubmitted the name, Brekiya for review on January 18, 2023, as part of the Class 2 Resubmission for NDA 215400.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on January 18, 2023.

- Intended Pronunciation: breh kee' yah
- Active Ingredient: dihydroergotamine mesylate
- Indication of Use: For the acute treatment of migraine headaches with or without aura and the acute treatment of cluster headache episodes.
- Route of Administration: subcutaneous
- Dosage Form: injection (autoinjector)
- Strength: 1 mg/mL
- Dose and Frequency: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.
- How Supplied: Available as a clear, colorless, sterile solution in a 1-mL prefilled syringe assembled in a single dose autoinjector containing 1 mg of dihydroergotamine mesylate per mL available as a carton pack of: (b) (4)
- Storage: Store at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Do not refrigerate or freeze. Protect from light. Retain in original pack until time of use.
- Reference Listed Drug/Reference Product: D.H.E 45 (dihydroergotamine mesylate) injection, USP (NDA 005929)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

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*

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

2.2.3 *Comments from Other Review Disciplines at Initial Review*

The Division of Neurology 2 (DN 2) did not forward any comments or concerns relating to Brekiya at the initial phase of the review.

2.2.4 *FDA Name Simulation Studies*

Eighty-seven practitioners participated in DMEPA's prescription studies for Brekiya. The responses did not directly overlap with any currently marketed products or any products in the pipeline.

One respondent in the voice study interpreted the proposed proprietary name as "Requia" which is a close hit to the currently marketed product, Requip. We further evaluated the name pair, Brekiya and Requip, in our previous review and found that there are sufficient orthographic, phonetic, and product characteristic differences between this name pair.^g Therefore, we found the risk of name confusion to be minimal, and we continue to agree with that determination.

One respondent in the voice study interpreted the proposed proprietary name as "Pracea" which is a close hit to the currently marketed product, Oracea. We further evaluated the name pair, Brekiya and Oracea, and find that there are sufficient orthographic, phonetic, and product characteristic differences between this name pair.

Orthographically, the names begin with different first letters (B vs. O) that look different. Additionally, Brekiya contains the upstroke letter "k" in the fourth position and the downstroke letter "y" in the sixth position, whereas Oracea does not contain any upstroke or downstroke letters which gives the names different shapes when scripted.

Phonetically, the first syllables (Breh vs. Or) and second syllables (kee vs. RAY) sound different when spoken.

^f USAN stem search conducted on March 4, 2023.

^g Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 SEP 21. Panorama No. 2021-1044724038.

Additionally, FDA’s Phonetic and Orthographic Computer Analysis (POCA) program calculates a combined score of 42% for this name pair suggesting there is low similarity between the names.

Furthermore, the following product characteristics may provide additional differentiation, if included: there is no direct overlap in strength (1 mg/mL versus 40 mg), dose and frequency (1 mg as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period (total weekly dosage should not exceed 6 mg) versus 40 mg once daily), dosage form (injection versus capsule) or route of administration (subcutaneous versus oral).

When all of the aforementioned mitigations are considered in totality, we find the risk of name confusion is minimal (see Appendix E).

Additionally, 13 respondents in the voice study omitted the beginning letter sound ‘B’.

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 49 names with the combined score of $\geq 55\%$ or individual orthographic or phonetic score of $\geq 70\%$. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed, and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified 3 names not previously analyzed. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search and the FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	0
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	4
Low similarity name pair: combined match percentage score $\leq 54\%$	0

^h POCA search conducted on March 4, 2023 in version 5.2.

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 4 names contained in Table 1 determined none of the names will pose a risk for confusion with Proposed Proprietary Name as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On April 6, 2023, DMEPA 2 communicated our determination to the Division of Neurology 2 (DN 2).

3 CONCLUSION

The proposed proprietary name, Brekiya, is conditionally acceptable.

If you have any questions or need clarifications, please contact Margee Webster, OSE project manager, at 240-402-0012.

3.1 COMMENTS TO AMNEAL PHARMACEUTICALS LLC (AMNEAL)

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

If any of the proposed product characteristics as stated in your submission, received on January 18, 2023, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. **Phonetic and Orthographic Computer Analysis (POCA)**

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

Drugs@FDA

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

RxNorm

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

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

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm

(<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html>).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.ⁱ

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

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

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

- 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, CernerRxNorm, 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.
 - 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 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.

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

- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a 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) and/or Office of Generic Drugs (OGD), ONDQA or OBP 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-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 ONDQA or OBP 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 reviewer 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.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
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 as 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 <u>with</u> overlapping or similar strengths or doses.

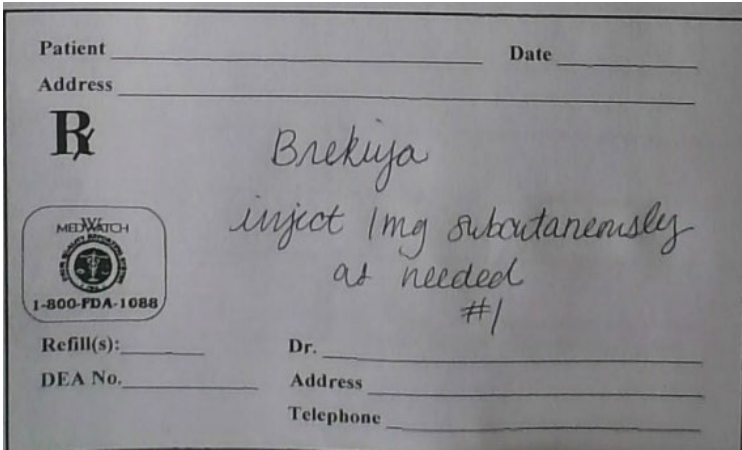
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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 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?	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?
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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.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Brekiya Study (Conducted on March 7, 2023)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Brekiya Inject 1 mg subcutaneously as needed #1
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Brekiya	

FDA Prescription Simulation Responses (Aggregate Report)

258 People Received Study 87 People Responded					
Study Name: Brekiya					
Total	24	22	21	20	87
INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
BRACHIA	0	0	1	0	1
BRAKEA	0	0	1	0	1
BRAKIA	0	0	1	0	1
BRECKIA	0	0	1	0	1
BREKEEYA	0	0	1	0	1
BREKIA	0	0	1	0	1

BREKIYA	23	22	1	19	65
BREKIYA INJECTION	1	0	0	0	1
BREKUJA	0	0	0	1	1
BRIKEA	0	0	1	0	1
PRACEA	0	0	1	0	1
RAKEA	0	0	1	0	1
RAKEYA	0	0	1	0	1
RAQUIA	0	0	1	0	1
REHKIA	0	0	1	0	1
REKIA	0	0	4	0	4
REKIYA	0	0	1	0	1
REQUIA	0	0	1	0	1
RYKEA	0	0	1	0	1
RYKIA	0	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is $\geq 70\%$)

No.	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.	N/A		

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	(b) (4) ***	55

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.	(b) (4) ***	56	This name pair has sufficient orthographic and phonetic differences.
2.	Oracea	42	Orthographically, the names begin with different first letters (B vs. O) that look different. Additionally, Brekiya contains the upstroke letter “k” in the fourth position and the downstroke letter “y” in the sixth position, whereas Oracea does not contain any upstroke or downstroke letters which gives the names different shapes when scripted.

No.	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
			Phonetically, the first syllables (Breh vs. Or) and second syllables (kee vs. RAY) sound different when spoken. Furthermore, the following product characteristics may provide additional differentiation, if included: there is no direct overlap in strength (1 mg/mL versus 40 mg), dose and frequency (1 mg as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period (total weekly dosage should not exceed 6 mg) versus 40 mg once daily), dosage form (injection versus capsule) or route of administration (subcutaneous versus oral).

Appendix F: Low Similarity Names (e.g., combined POCA score is $\leq 54\%$)

No.	Name	POCA Score (%)
1.	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.	N/A		

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.	(b) (4) ***	57

^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/

BEVERLY WEITZMAN
04/06/2023 02:39:59 PM

STEPHANIE L DEGRAW
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DANIELLE M HARRIS
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PROPRIETARY NAME MEMORANDUM

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:	January 7, 2022
Application Type and Number:	NDA 215400
Product Name and Strength:	Brekiya (dihydroergotamine mesylate) injection (autoinjector), 1 mg/mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sun Pharmaceutical Industries Limited (Sun Pharma)
PNR ID #:	2021-1044724326
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader (Acting):	Stephanie DeGraw, PharmD
DMEPA 2 Deputy Director:	Danielle Harris, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Brekiya, which was found unacceptable under NDA 215400 on September 21, 2021.^a The proposed proprietary name, Brekiya, was found to be vulnerable to medication errors due to confusion with another product, (b) (4) ***, under review at the time. Therefore, the ultimate acceptability of the proposed proprietary name, Brekiya, was dependent upon which underlying application was approved first.

Subsequently, Sun Pharma submitted the name, (b) (4) *** for review on October 14, 2021. However, Sun Pharma withdrew the name (b) (4) *** on December 10, 2021^b because the proposed name, Brekiya remains their preferred proposed proprietary name for this product. We also note that the other affected applicant holder of the conflicting name (b) (4) ** submitted an alternative name, (b) (4) *** for review on November 2, 2021.^c

We note that the goal date for NDA 215400 is January 19, 2022, whereas the underlying application for (b) (4) *** (b) (4) . Therefore, if the proposed proprietary name, Brekiya, is granted approval under NDA 215400 on or before January 19, 2022, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) ***.

Thus, Sun Pharma resubmitted their preferred proposed proprietary name, Brekiya, for review on December 10, 2021.

2 METHODS AND DISCUSSION

2.1 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, DMEPA 2 evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Additionally, DMEPA 2 searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The December 14, 2021 search of USAN stems did not find any USAN stems in the proposed proprietary name.

Finally, DMEPA 2 evaluated the status of the underlying application of the conflicting name, (b) (4) ***, and determined that if NDA 215400 for Brekiya is approved on or before the January 19, 2022, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) *** given the underlying application for (b) (4) *** (b) (4)

^a Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 SEP 21. Panorama No. 2021-1044724038.

^b Withdrawal of Proprietary name for (b) (4) *** (NDA 215400) available from docuBridge via: <\\CDSESUB1\evsprod\nda215400\0023\m1\us\cover-letter-pnr-withd.pdf>

^c Request for Proprietary name review for (b) (4) *** (IND (b) (4)) available from docuBridge via: <\\CDSESUB1\evsprod\ind112969\0097\m1\us\coverletter-0097.pdf>

Based upon our safety assessment of the proposed proprietary name, Brekiya, the application goal date for NDA 215400, and the status of the underlying application for (b) (4) ***, we find Brekiya conditionally acceptable at this time.

2.2 COMMUNICATION OF DMEPA 2 ANALYSIS

DMEPA 2 communicated our findings to the Division of Neurology 2 (DN 2) via e-mail on December 21, 2021.

3 CONCLUSIONS

We conclude that the proposed proprietary name, Brekiya, is acceptable.

If you have any questions or need clarifications, please contact Margee Webster, OSE project manager, at 240-402-0012.

3.1 COMMENTS TO SUN PHARMACEUTICAL INDUSTRIES LIMITED

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

If any of the proposed product characteristics as stated in your submission, received on December 10, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

If your application receives a complete response, please submit a new request for review of your proposed proprietary name when you respond to the application deficiencies.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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/s/

BEVERLY WEITZMAN
01/07/2022 09:27:04 AM

DANIELLE M HARRIS on behalf of STEPHANIE L DEGRAW
01/07/2022 11:34:03 AM

DANIELLE M HARRIS
01/07/2022 11:34:16 AM

PROPRIETARY NAME MEMORANDUM

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:	December 21, 2021
Application Type and Number:	NDA 215400
Product Name and Strength:	Brekiya ((b) (4) ***), injection (autoinjector), 1 mg/mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sun Pharmaceutical Industries Limited (Sun Pharma)
PNR ID #:	2021-1044724326
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader (Acting):	Stephanie DeGraw, PharmD
DMEPA 2 Deputy Director:	Danielle Harris, PharmD

1 INTRODUCTION

This memorandum is to reassess the proposed proprietary name, Brekiya, which was found unacceptable under NDA 215400 on September 21, 2021.^a The proposed proprietary name, Brekiya, was found to be vulnerable to medication errors due to confusion with another product, (b) (4) **, under review at the time. Therefore, the ultimate acceptability of the proposed proprietary name, Brekiya, was dependent upon which underlying application was approved first.

Subsequently, Sun Pharma submitted the name, (b) (4) ** for review on October 14, 2021. However, Sun Pharma withdrew the name (b) (4) *** on December 10, 2021^b because the proposed name, Brekiya remains their preferred proposed proprietary name for this product. We also note that the other affected applicant holder of the conflicting name (b) (4) *** submitted an alternative name, (b) (4) ** for review on November 2, 2021.^c

We note that the goal date for NDA 215400 is January 19, 2022, whereas the underlying application for (b) (4) *** (b) (4). Therefore, if the proposed proprietary name, Brekiya, is granted approval under NDA 215400 on or before January 19, 2022, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) ***.

Thus, Sun Pharma resubmitted their preferred proposed proprietary name, Brekiya, for review on December 10, 2021.

2 METHODS AND DISCUSSION

2.1 SAFETY ASSESSMENT

For re-assessment of the proposed proprietary name, DMEPA 2 evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. Additionally, DMEPA 2 searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The December 14, 2021 search of USAN stems did not find any USAN stems in the proposed proprietary name.

Finally, DMEPA 2 evaluated the status of the underlying application of the conflicting name, (b) (4) **, and determined that if NDA 215400 for Brekiya is approved on or before the January 19, 2022, this application approval will precede approval of the application with the conflicting proposed name, (b) (4) *** given the underlying application for (b) (4) *** (b) (4).

^a Weitzman, B. Proprietary Name Review for Brekiya (NDA 215400). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2021 SEP 21. Panorama No. 2021-1044724038.

^b Withdrawal of Proprietary name for (b) (4) *** (NDA 215400) available from docuBridge via: <\\CDSESUB1\evsprod\nda215400\0023\m1\us\cover-letter-pnr-withd.pdf>

^c Request for Proprietary name review for (b) (4) *** (IND (b) (4) available from docuBridge via: <\\CDSESUB1\evsprod\ind112969\0097\m1\us\coverletter-0097.pdf>

Based upon our safety assessment of the proposed proprietary name, Brekiya, the application goal date for NDA 215400, and the status of the underlying application for (b) (4) ***, we find Brekiya conditionally acceptable at this time.

2.2 COMMUNICATION OF DMEPA 2 ANALYSIS

DMEPA 2 communicated our findings to the Division of Neurology 2 (DN 2) via e-mail on December 21, 2021.

3 CONCLUSIONS

We conclude that the proposed proprietary name, Brekiya, is acceptable.

If you have any questions or need clarifications, please contact Margee Webster, OSE project manager, at 240-402-0012.

3.1 COMMENTS TO SUN PHARMACEUTICAL INDUSTRIES LIMITED

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

If any of the proposed product characteristics as stated in your submission, received on December 10, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

If your application receives a complete response, please submit a new request for review of your proposed proprietary name when you respond to the application deficiencies.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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/s/

BEVERLY WEITZMAN
12/21/2021 11:08:51 AM

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12/21/2021 11:20:00 AM

DANIELLE M HARRIS
12/21/2021 01:56:41 PM

PROPRIETARY NAME REVIEW

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

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

Date of This Review:	September 21, 2021
Application Type and Number:	NDA 215400
Product Name and Strength:	Brekiya (dihydroergotamine mesylate) injection (autoinjector), 1 mg/mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sun Pharmaceutical Industries Limited (Sun Pharma)
PNR ID #:	2021-1044724038
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Acting Team Leader:	Stephanie DeGraw, PharmD
DMEPA 2 Deputy Director:	Danielle Harris, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Brekiya, 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. Sun Pharma 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 June 24, 2021.

- Intended Pronunciation: breh kee' yah
- Active Ingredient: dihydroergotamine mesylate
- Indication of Use: For the acute treatment of migraine headaches with or without aura and the acute treatment of cluster headache episodes
- Route of Administration: subcutaneous
- Dosage Form: injection (autoinjector)
- Strength: 1 mg/mL
- Dose and Frequency: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.
- How Supplied: Available as a clear, colorless, sterile solution in a 1-mL prefilled syringe assembled in a single dose autoinjector containing 1 mg of dihydroergotamine mesylate per mL, in a carton pack
- Storage: Store at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Do not refrigerate or freeze. Protect from light. Retain in original pack until time of use.
- Reference Listed Drug/Reference Product: N/A

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name^a.

2.2.2 Components of the Proposed Proprietary Name

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

2.2.3 Comments from Other Review Disciplines at Initial Review

On July 21, 2021, the Division of Neurology 2 (DN 2) did not forward any comments or concerns relating to Brekiya at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

One hundred and thirteen practitioners participated in DMEPA's prescription studies for Brekiya. The responses did not directly overlap with any currently marketed products or any products in the pipeline.

One respondent in the voice study interpreted the proposed proprietary name as "Requia" which is a close hit to the currently marketed product, Requip. We further evaluated the name pair, Brekiya and Requip, and find that there are sufficient orthographic, phonetic, and product characteristic differences between this name pair.

Orthographically, Brekiya contains the letter "e" in the third position followed by an upstroke letter "k" in the fourth position, whereas Requip contains the downstroke letter "q" in the third position followed by the rounded letter "u" in the fourth position, which gives the names different shapes when scripted. Additionally the 2-letter string in the suffixes (ya vs. ip) provide additional differentiation.

Phonetically, Brekiya is 3 syllables whereas Requip is only 2 syllables. Additionally, the onset of the first syllables (Breh vs. Re) and second syllables (kee vs. quip) sound different when spoken.

Additionally, FDA's Phonetic and Orthographic Computer Analysis (POCA) program calculates a combined score of 44% for this name pair suggesting there is low similarity between the names.

Furthermore, the following product characteristics may provide additional differentiation, if included: there is no direct overlap in dosage form (injection versus tablet), route of administration (subcutaneous versus oral) and frequency of administration (taken as needed at 1-hour intervals versus three times daily).

When all of the aforementioned mitigations are considered in totality, we find the risk of name confusion is minimal (see Appendix F).

^a USAN stem search conducted on July 8, 2021.

Additionally, 19 respondents in the voice study omitted the beginning letter sound ‘B’.

Appendix B contains the results from the prescription simulation studies.

2.2.5 *Phonetic and Orthographic Computer Analysis (POCA) Search Results*

Our POCA search^b identified 45 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score $\geq 70\%$. These names are included in Table 1 below.

2.2.6 *Names Retrieved for Review Organized by Name Pair Similarity*

Table 1 lists the number of names retrieved from our POCA search and the FDA Prescription Simulation Study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	3
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	43
Low similarity name pair: combined match percentage score $\leq 54\%$	1

2.2.7 *Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities*

We determined forty-six (46) of the forty-seven (47) names will not pose a risk for confusion with Brekiya as described in Appendices C through H. However, the proposed proprietary name could be confused with another pending proprietary name, (b) (4) **. The rationale for the risk of confusion is described below.

Brekiya versus (b) (4) ***

The proposed proprietary name, Brekiya, may be confused with another pending proposed proprietary name that is also under review, (b) (4) (b) (4), due to orthographic similarities and overlapping product characteristics. The proposed indication for (b) (4) (b) (4)

Orthographically, Brekiya and (b) (4) *** are similar in length (7 letters versus (b) (4) letters), shape, and share (b) (4) identical letters ((b) (4) in similar or identical positions in the same sequence. The names begin with (b) (4)

^b POCA search conducted on July 8, 2021 in version 4.4.

Furthermore, the names share the same (b) (4)

We acknowledge that (b) (4) ** has (b) (4) and that Brekiya has an additional dotted letter 'i' in the fifth position. However, given the (b) (4), these differences may not be sufficient to mitigate the risk of confusion.

The similarity of this name pair is further supported by FDA's Phonetic and Orthographic Computer Analysis (POCA) program^c, which calculates a combined orthographic and phonetic score of 77% (individual orthographic score of 80%), suggesting that there is high similarity between these names.

Furthermore, since both names (b) (4) and are similar in length (7 letters *versus* (b) (4) letters), we are concerned that selection errors may occur by healthcare providers (b) (4). We have seen similar post marketing confusion between names that (b) (4). For example, confusion between (b) (4) occurred during electronic prescribing. (b) (4)

In addition to orthographic similarities, Brekiya and (b) (4) *** share overlapping product characteristics, which further increases the potential for wrong drug errors. Both products are proposed to be (b) (4). Therefore, (b) (4) may not be included on a prescription to help differentiate the products. Furthermore, we note overlap in the dosage (1 injection *versus* (b) (4) and a total of 3 mg in 24 hours *versus* (b) (4) between this name pair. Moreover, when comparing product characteristics, both Brekiya and (b) (4) *** can be ordered with the instructions (b) (4). We note the dose of Brekiya could vary (upwards of 3 subcutaneous injections (3 mg) in 24 hours) depending upon a patient's individual response to the proposed medication (i.e., resolution of migraine). Additionally, we note that (b) (4) ***, (b) (4)

We acknowledge that Brekiya and (b) (4) *** differ in strength (1 mg/mL *versus* (b) (4)), dosage form (prefilled syringe *versus* (b) (4)), route of administration (subcutaneous injection *versus* (b) (4)), and frequency of administration (one dose as needed for acute episode up to three doses in 24 hours *versus* (b) (4)). We are concerned that these differences may not

^c Institute for Safe Medication Practices. 2014 Jun 19. Safety briefs: Similar drug names confused. ISMP Med Saf Alert Acute Care. 19(12):1-3.

(b) (4)

prevent confusion between this name pair given the orthographic similarities of the names. We are aware of postmarketing reports of errors involving confusion between similarly named drug products, even when strength, dosage, and frequency of administration differ. For example, name confusion has been reported between Xeloda (capecitabine) and Xenical (orlistat) despite their differences in strength (120 mg *versus* 500 mg), dosage (divided dose of 2,500 mg/m² *versus* 120 mg), and frequency of administration (twice daily for two weeks, repeating the cycle three times with one drug-free week in-between *versus* three times daily).^e Additionally, we are aware of postmarketing reports of errors involving confusion between similarly named products despite differences in dosage form and routes of administration as seen in the case of Lantus (insulin glargine) and Latuda (lurasidone hydrochloride).^f

Furthermore, we recognize that the products have different indications (acute treatment of migraine headaches with or without aura and the acute treatment of cluster headache episodes *versus* (b) (4)), however, we are concerned that this difference in indication may not prevent confusion. Despite widespread recommendations only a small percentage of medications ordered include the indication.^g

Therefore, based on the totality of the information above, we find the proposed proprietary name, Brekiya, vulnerable to medication errors due to name confusion with (b) (4) ***.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Neurology 2 (DN 2). At that time we also requested additional information or concerns that could inform our review. On September 21, 2021, the Division of Neurology 2 (DN 2) stated no additional concerns with the proposed proprietary name, Brekiya.

3 CONCLUSION

The proposed proprietary name, Brekiya, is not acceptable from a safety perspective. The proposed proprietary name, Brekiya, is vulnerable to name confusion with (b) (4) ***. Therefore, the decision to deny the name will be communicated to Sun Pharmaceutical via letter (See Section 3.1).

If you have any questions or need clarifications, please contact Monique Killen, OSE project manager, at 240-402-1985.

3.1 COMMENTS TO SUN PHARMACEUTICAL INDUSTRIES LIMITED

We have completed our review of the proposed proprietary name, Brekiya, and have concluded that this name is unacceptable for the following reasons.

^e Institute for Safe Medication Practices. 1999 Sep 8. Safety Briefs. ISMP Med Saf Alert Acute Care. 4(18):1.

^f Institute for Safe Medication Practices. 2011 Aug 25. Include Purpose on Rx. ISMP Med Saf Alert Acute Care. 16(17):1-2.

^g Schiff GD Mirica MM, Dhavle AA, Galanter WL, Lambert B, Wright A. A Prescription for Enhancing Electronic Prescribing Safety. Health Affairs 2018; 37(11): 1877-1883.

Brekiya versus pending proprietary name

The proposed proprietary name, Brekiya, could result in medication errors due to the confusion with another product that is also under review. Therefore, the ultimate acceptability of your proposed proprietary name, Brekiya, is dependent upon which underlying application is approved first. If another product is approved prior to your product, with a name that would be confused with your proposed name Brekiya, you will be requested to submit another name.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

2. *Phonetic and Orthographic Computer Analysis (POCA)*

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

Drugs@FDA

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

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

APPENDICES

Appendix A

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

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.^h

^h National Coordinating Council for Medication Error Reporting and Prevention. <https://www.nccmerp.org/about-medication-errors> Last accessed 10/05/2020.

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

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

- 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, CernerRxNorm, 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.
 - 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 namesⁱ. 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 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

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

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 staff also conducts a 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) and/or Office of Generic Drugs (OGD), ONDQA or OBP 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-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. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP 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 reviewer 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.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
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 as 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 <u>with</u> overlapping or similar strengths or doses.

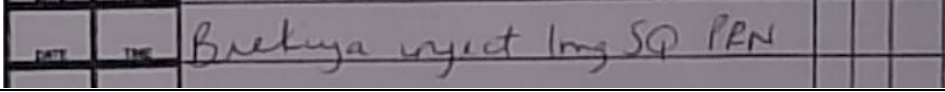
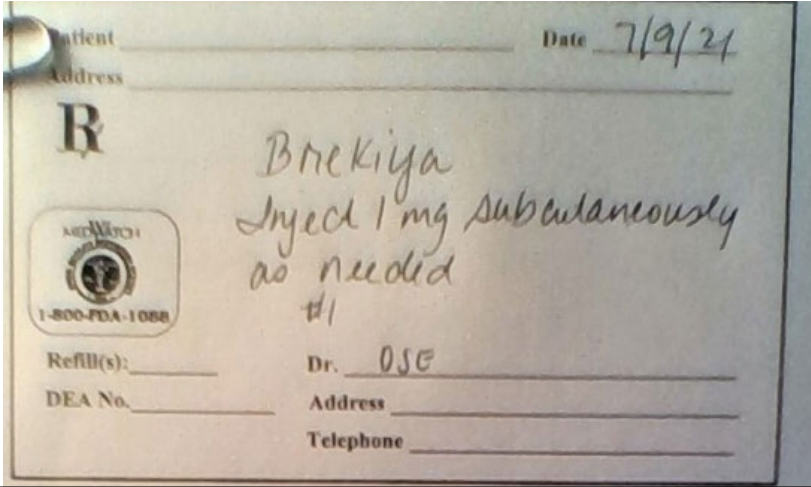
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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 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?	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?
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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.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Brekiya Study (Conducted on July 9, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Brekiya Inject 1 mg subcutaneously as needed #1
Outpatient Prescription: 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Brekiya	

FDA Prescription Simulation Responses (Aggregate Report)

265 People Received Study 113 People Responded					
Study Name: Brekiya					
Total	28	28	25	32	113
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
BRAKIA	0	0	2	0	2
BRAQEA	0	0	1	0	1
BRAQUIA	0	0	1	0	1
BRECEA	0	0	1	0	1

BREKEYA	0	0	0	3	3
BREKIYA	28	28	0	15	71
BREKIYA INJECTION	0	0	0	1	1
BREKUJA	0	0	0	1	1
BREKUYA	0	0	0	3	3
BREKYA	0	0	0	6	6
BRETIYA	0	0	0	1	1
BREVKIA	0	0	1	0	1
BRKIYA	0	0	0	1	1
BRYKIYA	0	0	0	1	1
RACKIA	0	0	1	0	1
RACKIYA	0	0	1	0	1
RAKEA	0	0	1	0	1
RAKEIA	0	0	1	0	1
RAKIA	0	0	6	0	6
RAKYA	0	0	1	0	1
RAQIA	0	0	1	0	1
RAQUIA	0	0	4	0	4
RAQUYA	0	0	1	0	1
REKIA	0	0	1	0	1
REQUIA	0	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is $\geq 70\%$)

No.	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.	Brekiya	100	Proposed proprietary name that is the subject of this review.
2.	(b) (4) ***	70	Proposed proprietary name for IND (b) (4) was withdrawn by the Applicant on May 31, 2018. NDA 212194 approved under proprietary name, Givlaari.

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

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

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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.	(b) (4) ***	65	This name pair has sufficient orthographic and phonetic differences.

	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
			Orthographically, the name pair begins with different first letters (B versus (b) (4) that look different. Additionally, Brekiya contains the additional rounded letter ‘r’ in prefix which is not present in (b) (4) *** which provides additional differentiation. Lastly, Brekiya contains the downstroke letter ‘y’ in the suffix, whereas (b) (4) *** contains the (b) (4) letter (b) (4) (b) (4) which gives the names different shapes when scripted. Furthermore, the following product characteristics may provide additional differentiation if included: there is no direct overlap in strength (1 mg/mL versus (b) (4)), dose and frequency (1 mg as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period (total weekly dosage should not exceed 6 mg) versus (b) (4) or route of administration (subcutaneous versus (b) (4))
2.	Bekyree	64	This name pair has sufficient orthographic and phonetic differences. Orthographically, Brekiya contains the rounded ‘r’ in the prefix between the letters ‘B’ and ‘k’ which is not present in Bekyree which may provide some

	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
			differentiation. Additionally, the suffixes (ya vs. ree) look sufficiently different. Furthermore, the following product characteristics may provide additional differentiation if included: there is no direct overlap in strength (1 mg/mL versus 0.15 mg/0.02 mg/0.01 mg), frequency (taken as needed at 1-hour intervals versus once daily),dosage form (injection versus tablet) or route of administration (subcutaneous versus oral).
3.	Breyna***	64	This name pair has sufficient orthographic and phonetic differences. Orthographically, the shapes of the names look sufficiently different when scripted. Brekiya contains the upstroke letter 'k' in the fourth position, whereas Breyna*** does not contain any upstroke letters. Additionally, Brekiya contains the dotted letter 'i' in the fifth position, whereas Breyna contains the rounded letter 'n' in the fifth position. Lastly, both contain the downstroke letter 'y', however it appears in different positions of the name pair which provides additional differentiation. Phonetically, Brekiya contains 3 syllables whereas Breyna is only 2

	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
			syllables. Additionally, the second syllables (kee' vs. nah) sound different when spoken. Furthermore, Brekiya is available in one strength (1 mg/mL), whereas Breyna*** is available in two strengths (80 mcg/4.5 mcg and 160 mcg/4.5 mcg) which must be specified on the prescription and the strengths do not overlap. Additionally, the following product characteristics may provide additional differentiation if included: there is no direct overlap in dose and frequency (1 mg as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period (total weekly dosage should not exceed 6 mg) versus 2 inhalations twice daily), dosage form (injection versus inhalation) or route of administration (subcutaneous versus oral).
4.	Brineura	64	This name pair has sufficient orthographic and phonetic differences.
5.	Brukina	64	This name pair has sufficient orthographic and phonetic differences.
6.	Biokera	62	This name pair has sufficient orthographic and phonetic differences.
7.	Bryhali	61	This name pair has sufficient orthographic and phonetic differences.
8.	Breztri	60	This name pair has sufficient orthographic and phonetic differences.
9.	(b) (4) ***	60	This name pair has sufficient orthographic and phonetic differences.

	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
10.	Bricanyl	59	This name pair has sufficient orthographic and phonetic differences.
11.	Qbrexza	57	This name pair has sufficient orthographic and phonetic differences
12.	Bravelle	56	This name pair has sufficient orthographic and phonetic differences
13.	Brevital	56	This name pair has sufficient orthographic and phonetic differences
14.	Breyanzi	56	This name pair has sufficient orthographic and phonetic differences. Orthographically, Brekiya contains the upstroke letter ‘k’ at the beginning of the infix, whereas Breyanzi contains the downstroke letter ‘y’ at the beginning of the infix which gives the names different shapes when scripted. Furthermore, the following product characteristics may provide additional differentiation if included: there is no direct overlap in dose and frequency (1 mg as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period (total weekly dosage should not exceed 6 mg) versus single dose containing a target of $(b) (4) \times 10^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) two to seven days after completion of lymphodepleting chemotherapy), or route of administration (subcutaneous versus intravenous infusion).

	Proposed name: Brekiya Established name: dihydroergotamine mesylate Dosage form: injection (autoinjector) Strength(s): 1 mg/mL Usual Dose: 1 mg subcutaneously as needed at 1-hour intervals up to a total dose of 3 mg in a 24-hour period. The total weekly dosage should not exceed 6 mg.	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
			Furthermore, Breyanzi is unlikely to be dispensed from a pharmacy as it is patient-specific Chimeric Antigen Receptor (CAR) T cell product that consists of two individually formulated CD4+CAR+ and CD8+CAR+ frozen T cell suspensions prepared in patient-specific 5 mL infusion vials stored frozen (-130° C). It is shipped in liquid nitrogen to be administered by trained qualified personal. A patient's name and identifier will be on each dose because patients receiving Breyanzi undergo leukapheresis to enable patient-specific product generation.
15.	Brian Care	56	This name pair has sufficient orthographic and phonetic differences.
16.	Bronkaid	56	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
1.	Requip	44

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.	(b) (4) ***	67	Proposed proprietary name for IND (b) (4) found unacceptable by DMEPA (OSE Review #2017-16491499 dated November 3, 2017). NDA 210861 and NDA 211710 approved under proprietary name, Vitrakvi.
2.	Brexin L.A.	66	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
3.	Barri-Care	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
4.	(b) (4) ***	60	Proposed proprietary name for IND (b) (4) was found unacceptable by DMEPA (OSE # 2017-12412628 dated February 23, 2017). NDA 210557 approved under proprietary name, Vyleesi.
5.	Bretylate	59	International product marketed in Singapore and formerly marketed in Ireland, France, Australia, United Kingdom, Netherlands, Canada, Belgium, and Israel.
6.	(b) (4)		
7.	(b) (4) ***	58	Proposed proprietary name for IND (b) (4) found unacceptable by DMEPA (OSE# 2017-13946987 dated September 8, 2017). NDA 209355 approved under proprietary name, Bryhali.
8.	B-12 Resin	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
9.	(b) (4) ***	57	Proposed proprietary name for IND (b) (4) was withdrawn by the Applicant on December 21, 2017. BLA 761104 approved under proprietary name, Lumoxiti.
10.	Ubretid	57	International product marketed and formerly marketed in multiple countries outside the US.
11.	Bretylol	56	Brand discontinued with no generic equivalents available. NDA 017954 withdrawn FR effective 06/10/1999.
12.	Brexidol	56	International product marketed in Italy, Norway, and Sweden and formerly marketed in Germany, Canada, Switzerland, United Kingdom, Finland, Denmark, and Austria.

No.	Name	POCA Score (%)	Failure preventions
13.	Broxil	55	International product marketed in the Netherlands and formerly marketed in the United Kingdom.
14.	(b) (4) ***	55	Proposed proprietary name for IND 122464 found unacceptable by DMEPA (OSE #2019-34043132 dated December 18, 2019). NDA 213189 approved under proprietary name, Klisyri.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^j.

No.	Name	POCA Score (%)
1.	Tresiba	62
2.	Tripedia	58
3.	Droxia	58
4.	(b) (4) ***	57
5.	Rezira	56
6.	Rukobia	56
7.	Fibryga	56
8.	Verkazia***	56
9.	Tremfya	56
10.	Trexima	56
11.	Meridia	56
12.	Propecia	56

^j 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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