CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761134Orig1s000

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:	August 22, 2023
Application Type and Number:	BLA 761134
Product Name and Strength:	Ryzneuta (efbemalenograstim alfa- vuxw)[a] injection, 20 mg/mL
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Evive Biotechnology (Singapore) PTE. LTD. (Evive)
PNR ID #:	2021-1044723895-1
DMEPA 2 Safety Evaluator:	Sue Black, PharmD
DMEPA 2 Acting Team Leader (Acting):	Nicole Iverson, PharmD, BCPS
DMEPA 2 Acting Associate Director for Nomenclature and Labeling (Acting):	Hina Mehta, PharmD

[a] The nonproprietary name, efbemalenograstim alfa-vuxw, was found conditionally acceptable on January 06, 2022.

Contents

1 INTRODUCTION

This memorandum is initiated by DMEPA 2 to reassess the proposed proprietary name, Ryzneuta, which was found conditionally acceptable under IND 112198 and BLA 761134 on June 9, 2021[b]. The Agency was unable to conduct inspection of the Evive Biotechnology manufacturing facility due to travel restrictions at that time; therefore, the Agency deferred action on the application until an inspection can be completed. As the Office of Pharmaceutical Manufacturing Assessment (OPMA) resumed foreign inspections, the Agency was able to conduct an inspection of the facility from May 30, 2023 to June 7, 2023. Therefore, the marketing application review process was resumed. Given the amount of the time since our previous review, we are re-reviewing the name from a safety perspective. We note that all the product characteristics remain the same.

2 RESULTS

2.1 SAFETY ASSESSMENT

The following aspects were considered in the safety re-evaluation of the proposed proprietary name, Ryzneuta.

2.1.1 United States Adopted Names (USAN) Search

We searched the USAN stem list to determine if the proposed proprietary name contains any USAN stems as of the last USAN updates. The July 17, 2023 search of USAN stems did not find any USAN stems in the proposed proprietary name, Ryzneuta

2.1.2 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[c] identified 50 names with the combined score of ≥55% or individual orthographic or phonetic score of ≥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.

2.1.3 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists 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.

[b] Straka, M. Proprietary Name Review for Ryzneuta (IND 112198 and BLA 761134). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 JUN 09. PNR ID No. 2021-1044723828 and 2021-1044723895.

[c] POCA search conducted on July 14, 2023 in version 5.2.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	3
Low similarity name pair: combined match percentage score ≤54%	0

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

Our analysis of the 3 names contained in Table 1 determined none of the names will pose a risk for confusion with Ryzneuta as described in Appendices C through H.

3 CONCLUSION

Our re-assessment did not identify any names that represent a potential source of drug name confusion. Therefore, we maintain that the proposed proprietary name, Ryzneuta, is conditionally acceptable.

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. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. 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, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

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

Using the criteria outlined in the check list (Table 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[d]. 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.

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

- 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.

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 ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?

Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is 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?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

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

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%) – N/A

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose – N/A

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

No.	**Proposed name:** Ryzneuta **Established name:** efbemalenograstim alfa- vuxw **Dosage form:** injection **Strength(s):** 20 mg/mL **Usual Dose:** 20 mg as a single dose once per chemotherapy cycle.	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)***	61	(b) (4)
2.	Ryzumvi***	57	This name pair has sufficient orthographic and phonetic differences

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

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

No.	Name	POCA Score (%)	Failure preventions
1.	(b) (4)***	56	Proposed proprietary name withdrawn by the Applicant. The proprietary name, (b) (4)***, was found conditionally acceptable for NDA (b) (4) however, the application received a Complete Response Letter on July 18, 2023.

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

[e] 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/

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HINA S MEHTA
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SUFFIX REVIEW FOR NONPROPRIETARY NAME

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:	1/6/2022
Responsible OND Division:	Division of Non-Malignant Hematology (DNH)
Application Type and Number:	BLA 761134
Product Name and Strength:	Ryzneuta (efbemalenograstim alfa-vuxw) injection, 20 mg/mL
Product Type:	Combination Product (Biologic-Device)
Applicant/Sponsor Name:	Evive Biotechnology Singapore PTE LTD (Evive)
Nexus NPNS ID #:	2021-19
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Director:	Danielle Harris, PharmD

1 PURPOSE OF REVIEW

This review summarizes our evaluation of the four-letter suffix for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761134.

1.1 Regulatory History

Evive was notified of the Agency's intention to designate a nonproprietary name that includes a four-letter distinguishing suffix that is devoid of meaning for their product in an Advice Letter[a].

2 ASSESSMENT OF THE NONPROPRIETARY NAME

efbemalenograstim alfa-vuxw

FDA generated a four-letter suffix, -vuxw. This suffix was evaluated using the principles described in the applicable guidance[b].

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

3 COMMUNICATION OF DMEPA 2 ANALYSIS

These findings were shared with OPDP. On December 21, 2021, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Non-Malignant Hematology (DNH) on December 27, 2021.

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[a] Harris, D. General Advice Letter for BLA 761134. Silver Spring (MD): FDA, CDER, OSE, DMAMES (US) 2021 Apr 19.
[b] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

4 CONCLUSION

We find the suffix -vuxw acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to efbemalenograstim alfa-vuxw. DMEPA 2 will communicate our findings to the Applicant via letter.

4.1 Recommendation for Evive Biotechnology Singapore PTE LTD

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

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CARLOS M MENA-GRILLASCA
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DANIELLE M HARRIS
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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:	June 9, 2021
Application Type and Number:	IND 112198 and BLA 761134
Product Name and Strength:	Ryzneuta (efbemalenograstim alfa-xxxx)[a] injection, 20 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Evive Biotechnology (Singapore) Ltd. (Evive)
PNR ID #:	2021-1044723828 and 2021-1044723895
DMEPA Safety Evaluator:	Maximilian Straka, PharmD, FISMP
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director of Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, FISMP

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

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Ryzneuta, 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. Evive submitted an external name study, conducted by (b) (4) for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 19, 2021 and March 30, 2021.

- Intended Pronunciation: raiz ´nu tah
- Nonproprietary Name: efbemalenograstim alfa-xxxx
- Indication of Use: Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
- Route of Administration: subcutaneous
- Dosage Form: injection
- Strength: 20 mg/mL
- Dose and Frequency: 20 mg as a single dose once per chemotherapy cycle.
- How Supplied: Ryzneuta is provided in a dispensing pack containing one (b) (4) prefilled syringe. Each prefilled syringe of Ryzneuta contains 1 mL of a sterile, preservative free, 20 mg/mL solution for SC injection.
- Storage: Ryzneuta should be stored refrigerated at 2° to 8°C

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Ryzneuta would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Non-Malignant Hematology (DNH) concurred with the findings of OPDP's assessment for Ryzneuta.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

Evive did not provide a derivation or intended meaning for the proposed proprietary name, Ryzneuta, 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 April 15, 2021, the Division of Non-Malignant Hematology (DNH) did not forward any comments or concerns relating to Ryzneuta at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Sixty-two (62) practitioners participated in DMEPA's prescription studies for Ryzneuta.

In the computerized provider order entry (CPOE) study, one participant entered an incorrect sequence of letters, 'ryn' instead of 'ryz, when searching for the study name, which generated a pick list that did not contain the proposed study name Ryzneuta. After 20 seconds passed, the participant then incorrectly selected the name 'Rynessa', suggesting that the participant selected a random name in order to proceed with the simulation study. Thus, in this case, the study response is unlikely to be representative of a plausible CPOE based risk. In addition, Rynessa was identified in our POCA search in the RxNorm database. We were unable to find the product characteristics in commonly used drug databases. We evaluate this name in Appendix G.

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[c] identified 47 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥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 (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

[b] USAN stem search conducted on April 19, 2021.

[c] POCA search conducted on April 19, 2021 in version 4.4.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	44
Low similarity name pair: combined match percentage score ≤54%	4

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

Our analysis of the 49 names contained in Table 1 determined none of the names will pose a risk for confusion with Ryzneuta as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Non-Malignant Hematology (DNH). At that time we also requested additional information or concerns that could inform our review. On June 1, 2021, the Division of Non-Malignant Hematology (DNH) stated no additional concerns with the proposed proprietary name, Ryzneuta.

3 CONCLUSION

The proposed proprietary name, Ryzneuta, is acceptable.

If you have any questions or need clarifications, please contact Linda Wu, OSE project manager, at 240-402-5120.

3.1 COMMENTS TO EVIVE BIOTECHNOLOGY (SINGAPORE) LTD.

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

If any of the proposed product characteristics as stated in your submission, received on March 30, 2021, 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

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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. [d]

[d] 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 ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 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[e]. 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

[e] 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 ≥ 70%).

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

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

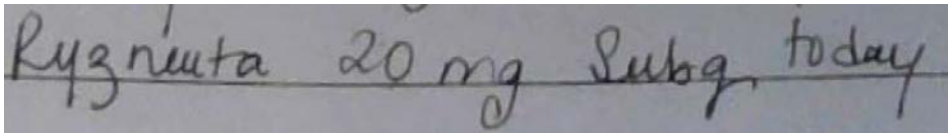
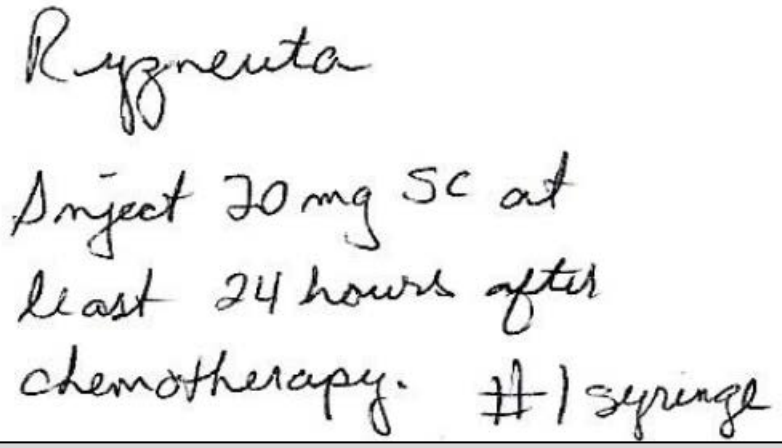
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is 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?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

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

Appendix B: Prescription Simulation Samples and Results

Figure 1. Ryzneuta Study (Conducted on April 2, 2021)

Handwritten Medication Order/Prescription	**Verbal Prescription**
Medication Order:  	Ryzneuta Inject 20 mg subcutaneously at least 24 hours after chemo therapy Dispense # 1 syringe
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Ryzneuta	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Ryzneuta

As of Date 4/30/2021

209 People Received Study

62 People Responded

Study Name: Ryzneuta

Total	13	21	15	13	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
REISNUTRA	0	0	1	0	1
RIBNUTA	0	0	1	0	1
RISENEUTRA	0	0	1	0	1
RISENIQA	0	0	1	0	1
RIVNUTA	0	0	1	0	1
RIZNUCHA	0	0	1	0	1
RYNESSA	0	1	0	0	1
RYSNUTA	0	0	3	0	3
RYTNEUTA	0	0	1	0	1
RYVNUTA	0	0	1	0	1
RYZNEUTA	9	20	1	12	42
RYZNEUTA INJECTION	1	0	0	0	1
RYZNEUTRA	3	0	0	1	4
RYZNEWTA	0	0	1	0	1
RYZNUTA	0	0	1	0	1
VIZNUTA	0	0	1	0	1

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

No.	**Proposed name:** Ryzneuta **Established name:** efbemalenograstim alfa-xxxx **Dosage form:** injection **Strength(s):** 20 mg/mL **Usual Dose:** 20 mg as a single dose once per chemotherapy cycle.	**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.	Ryzneuta***	100	This name is the subject of this review.

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

No.	Name	POCA Score (%)
1.	(b) (4) ***	58
2.	Ranexa	56

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

No.	**Proposed name:** Ryzneuta **Established name:** efbemalenograstim alfa-xxxx **Dosage form:** injection **Strength(s):** 20 mg/mL **Usual Dose:** 20 mg as a single dose once per chemotherapy cycle.	**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	(b) (4)

No.	**Proposed name:** Ryzneuta **Established name:** efbemalenograstim alfa-xxxx **Dosage form:** injection **Strength(s):** 20 mg/mL **Usual Dose:** 20 mg as a single dose once per chemotherapy cycle.	**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**
			(b) (4)
2.	Ryvent	64	This name pair has sufficient orthographic and phonetic differences.
3.	Razadyne	60	This name pair has sufficient orthographic and phonetic differences.
4.	(b) (4) ***	58	This name pair has sufficient orthographic and phonetic differences.
5.	Revonto	58	This name pair has sufficient orthographic and phonetic differences.
6.	Oral-B neutra	58	This name pair has sufficient orthographic and phonetic differences.
7.	Relenza	56	This name pair has sufficient orthographic and phonetic differences.
8.	Roszet***	56	This name pair has sufficient orthographic and phonetic differences.
9.	Ryna C	56	This name pair has sufficient orthographic and phonetic differences.
10.	Ryzolt	56	This name pair has sufficient orthographic and phonetic differences. We acknowledge that the proposed name Ryzneuta begins with the letter string “Ryz” that overlaps with letters in Ryzolt, which raises potential risk for CPOE selection error. However, given there's no overlap in strength (20 mg/mL vs. 100 mg, 200 mg, and 300 mg), dose (20 mg vs. 1 tablet), route (subcutaneous vs. oral), dosage form (injection vs. tablets), and frequency of administration (once per chemotherapy cycle vs. once daily), the unlikelihood that all 5 different product

No.	**Proposed name:** Ryzneuta **Established name:** efbemalenograstim alfa-xxxx **Dosage form:** injection **Strength(s):** 20 mg/mL **Usual Dose:** 20 mg as a single dose once per chemotherapy cycle.	**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**
			characteristics will be overlooked during a computerized prescriber order entry is minimized; thus we believe the risk of CPOE selection error is minimized in this case.
11.	Brineura	56	This name pair has sufficient orthographic and phonetic differences.
12.	Zebutal	56	This name pair has sufficient orthographic and phonetic differences.
13.	Reyataz	55	This name pair has sufficient orthographic and phonetic differences.
14.	Rezamid	55	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.	Systane Ultra	52
2.	Rizatriptan	46
3.	Zetran	46
4.	Neupogen	29

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.	Rynatan	68	Name identified in RxNorm database. Product deactivated per RedBook with no generic equivalent available.
2.	Rynesa	67	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
3.	Rynessa	65	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

No.	Name	POCA Score (%)	Failure preventions
4.	(b) (4)***	58	Proposed proprietary name (b) (4)*** for IND 064119 was found unacceptable by DMEPA (OSE # 2017-12412628). NDA 210557 approved under the proprietary name, Vyleesi.
5.	Rennet	58	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases.
6.	(b) (4)***	58	Proposed proprietary name for IND 112311 found unacceptable by DMEPA (OSE# 2017-17830701). Product approved under the NDA 213464 with the proprietary name Lampit.
7.	Ryzodeg	58	Formerly marketed in the US, discontinued with no generic equivalents available in the US. Currently marketed internationally.
8.	Ryzodeg 70/30	58	Formerly marketed in the US, discontinued with no generic equivalents available in the US. Currently marketed internationally.
9.	Trynate	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
10.	Radent	56	Foreign product name formerly marketed in the New Zealand.
11.	Renotec	56	Brand discontinued with no generic equivalents available. NDA 017045 withdrawn FR effective 03/13/2009.
12.	(b) (4)***	56	Proposed proprietary name for IND (b) (4) found unacceptable by DMEPA (OSE Review# (b) (4) (b) (4)). IND (b) (4) is pending and no new names have been submitted.
13.	Respi-Tann	56	Name identified in RxNorm database. Product is deactivated (per Redbook) and no generic equivalents are available.
14.	(b) (4)***	56	Proposed proprietary name for BLA (b) (4) found unacceptable by CBER's Advertising and Promotional Labeling Branch (APLB) on 9/16/2015. The Applicant submitted the proposed name, (b) (4)***, which was found unacceptable by APLB on 1/25/2016. No new proposed proprietary name has been submitted.
15.	Rinatec	56	International product marketed in Ireland and the United Kingdom.

No.	Name	POCA Score (%)	Failure preventions
16.	(b) (4)***	56	Proposed proprietary name for NDA (b) (4) (b) (4) found unacceptable by DMEPA (OSE# (b) (4)). NDA (b) (4) was withdrawn by the Applicant on August 14, 2012.

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

No.	Name	POCA Score (%)
1.	Vyzulta	62
2.	Fylnetra***	60
3.	Erycette	57
4.	Arnuity	56
5.	Crysvita	56
6.	Leventa	56
7.	(b) (4)***	56
8.	Orlenta	56
9.	Trinessa	56
10.	Dura-Vent/A	55
11.	Trental	55
12.	(b) (4)***	55

[f] 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/

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