

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761161Orig1s000

PROPRIETARY NAME REVIEW(S)

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:	2/9/2023
Responsible OND Division:	Division of Rare Diseases and Medical Genetics (DRDMG)
Application Type and Number:	BLA 761161
Product Name and Strength:	Elfabrio (pegunigalsidase alfa-iwxj) injection, 20 mg/10 mL (2 mg/mL)
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Chiesi Farmaceutici S.p.A. (Chiesi)
Nexus NPNS ID #:	2022-142
DMAMES Biologics Suffix Specialist:	Carlos M Mena-Grillasca, BS Pharm
DMEPA 2 Director:	Danielle Harris, PharmD

1 PURPOSE OF REVIEW

This review is to reassess the FDA-generated suffix, -iwxj, for BLA 761161, which was found conditionally acceptable on October 20, 2020^a, for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761161.

1.1 Regulatory History

FDA generated a four-letter suffix, -iwxj, for BLA 761161 on October 20, 2020^a. However, BLA 761161 received a Complete Response (CR) letter on April 27, 2021^b. Thus, Chiesi submitted a Class 2 Resubmission on November 9, 2022.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

We reassessed the previously generated four-letter suffix, -iwxj, using the principles described in the applicable guidance^c.

We determined that the FDA-generated suffix -iwxj, 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 February 8, 2023, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA 2 also communicated our findings to the Division of Rare Diseases and Medical Genetics (DRDMG) on February 9, 2023.

^a Mena-Grillasca, C. Nonproprietary Name Suffix Review for pegunigalsidase alfa-iwxj (BLA 761161). Silver Spring (MD): FDA, CDER, OSE, OMEPRM, DMEPA (US); 2020 Oct 20. RCM No.: 2020-1625.

^b Joffe, H.V. Complete Response (BLA 761161). Silver Spring (MD): FDA, CDER, OND (US); 2021 Apr 27.

^c 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 -iwxj acceptable and recommend the nonproprietary name pegunigalsidase alfa-iwxj be used throughout the labels and labeling.

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
02/09/2023 02:18:18 PM

DANIELLE M HARRIS
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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 3, 2023
Application Type and Number:	BLA 761161
Product Name and Strength:	Elfabrio (pegunigalsidase alfa-iwxj) injection, 20 mg/10 mL (2 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Chiesi Farmaceutici S.p.A. (Chiesi Farmaceutici)
PNR ID #:	2022- 1044724839
DMEPA 2 Safety Evaluator:	Sali Mahmoud, PharmD, BCPS
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD, BCCCP
DMEPA 2 Deputy Director:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Elfabrio, 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. Chiesi Farmaceutici submitted an external name study, previously conducted by (b) (4) for this proposed proprietary name. The external study was evaluated in our previous review of the name Elfabrio.^a

1.1 REGULATORY HISTORY

Protalix Ltd, has been actively engaged in co-development of pegunigalsidase alfa injection with the aforementioned Sponsor Chiesi, USA. Protalix, Ltd previously submitted the proposed proprietary name, Elfabrio on July 26, 2019, under IND 110161. However, we found the name, Elfabrio unacceptable due to spelling, orthographic and phonetic similarities, and shared product characteristics with the proprietary name, (b) (4) under IND 110161 on January 15, 2020^a. Hence, Protalix submitted the name, (b) (4) for review on January 25, 2020 under IND 110161 and Chiesi submitted the name, (b) (4) for review on May 27, 2020 under BLA 761161. On July 16, 2020, we found the name, (b) (4) conditionally acceptable under IND 110161 and BLA 761161^b.

During our label and labeling review of BLA 761161, Chiesi noted that their preferred proposed name was Elfabrio for their product. Therefore, we requested Chiesi to withdraw their conditionally accepted name, (b) (4) and resubmit their preferred name, Elfabrio, under BLA 761161^c. Thus, Chiesi withdrew their conditionally approved name, (b) (4) and resubmitted the proposed proprietary name Elfabrio for review on November 19, 2020. On February 11, 2021 Elfabrio was found acceptable under BLA 761161^d. On April 27, 2021 the application received a Complete Response letter (CRL)^e due to facility issues and presence of alternative therapies for treatment for Fabry disease. On November 9, 2022 Chiesi resubmitted BLA 761161 with new and amended contents addressing the deficiencies listed in the CRL.

Thus, Chiesi Farmaceutici resubmitted the name, Elfabrio, for review on November 9, 2022.

^a Abraham, S. Proprietary Name Review for Elfabrio (IND 110161). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Jan 15. Panorama No. 2019-33427979

^b Abraham, S. Proprietary Name Review for (b) (4) (IND 110161 and BLA 761161). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Jul 16. Panorama No. 2020-37412071 (IND) and 2020-40218398 (BLA).

^c Sun, S. Proprietary Name Request Acknowledgement/Withdrawal (BLA 761161). Silver Spring (MD): FDA, CDER, OSE (US); 2020 Nov 9. Panorama No. 2020-40218398.

^d Abraham, S. Proprietary Name Review for Elfabrio (BLA 761161). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 FEB 11. Panorama No: 2020-43995827.

^e Joffe, H. Complete Response for Elfabrio. Silver Spring (MD): FDA, CDER, DRDMG (US); 2021 APR 27. BLA 761161.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 9, 2022.

- Intended Pronunciation: El fa' bree oh
- Nonproprietary Name: pegunigalsidase alfa-iwxj
- Indication of Use: treatment of adults with a confirmed diagnosis of Fabry disease
- Route of Administration: intravenous
- Dosage Form: injection
- Strength: 20 mg/10 mL (2 mg/mL)
- Dose and Frequency: 1 mg/kg administered every 2 weeks (b) (4)
- How Supplied: 20 mg/10 mL (2 mg/mL) solution in a single-dose vial. Cartons contain 1, 5, or 10 single dose vials.
- Storage: Refrigerate at 2°C to 8°C (36°F to 46°F). Do not freeze or shake.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Elfabrio 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 Elfabrio. The Division of Rare Diseases and Medical Genetics (DRDMG) did not comment on the findings of OPDP's assessment for Elfabrio.

2.2 SAFETY ASSESSMENT

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

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

Chiesi Farmaceutici did not provide a derivation or intended meaning for the proposed proprietary name, Elfabrio, in their submission. This proprietary name is comprised of a single

^f USAN stem search conducted on November 30, 2022.

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

Division of Rare Diseases and Medical Genetics (DRDMG) did not forward any comments or concerns relating to Elfabrio at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-seven (n= 87) practitioners participated in DMEPA's prescription studies for Elfabrio. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[§] identified 66 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. (b) (4)

None of the other product characteristics have changed. We considered these changes in our re-evaluation of the previous names 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 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. 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 $\leq 69\%$	7
Low similarity name pair: combined match percentage score $\leq 54\%$	0

[§] POCA search conducted on November 30, 2022 in version 5.2.

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

Our analysis of the 7 names contained in Table 1 determined none of the names will pose a risk for confusion with Elfabrio as described in Appendices C through H.

2.2.8 Communication of DMEPA's Determination

On February 3, 2023, DMEPA 2 communicated our determination to the Division of Rare Diseases and Medical Genetics (DRDMG).

3 CONCLUSION

The proposed proprietary name, Elfabrio, is conditionally acceptable.

If you have any questions or need clarifications, please contact Su-Lin Sun, OSE project manager, at 301-796-0036.

3.1 COMMENTS TO CHIESI FARMACEUTICI S.P.A.

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

If any of the proposed product characteristics as stated in your submission, received on November 9, 2022, 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.^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.

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.

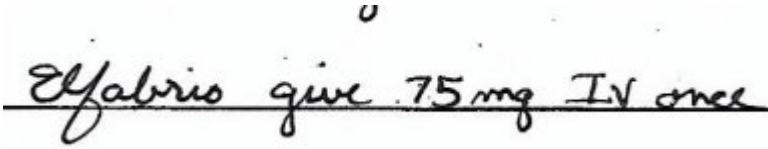
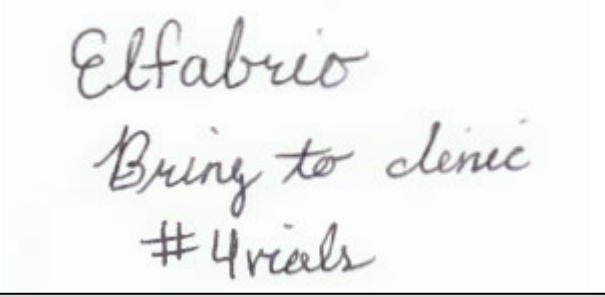
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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. Elfabrio Study (Conducted on December 6, 2022)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Elfabrio Bring to clinic. Dispense 4 vials
<u>Outpatient Prescription:</u> 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font) Elfabrio	

FDA Prescription Simulation Responses (Aggregate Report)

Study Name: Elfabrio
 260 People Received Study
 87 People Responded

Study Name: Elfabrio

Total 22 21 23 21

INTERPRETATION	INPATIENT	CPOE	VOICE	OUTPATIENT	TOTAL
ALFABRIO	0	0	1	0	1
EFFABRIO	2	0	0	1	3
EFLABRIO	1	0	0	0	1
ELFABRIO	17	21	17	20	75
ELFABRIS	1	0	0	0	1
ELFRABIO	0	0	1	0	1
EYOBRIO	1	0	0	0	1
HELFABRIO	0	0	2	0	2
OFABRIO	0	0	1	0	1
OLFABRIO	0	0	1	0	1

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

No.	Proposed name: Elfabrio Established name: pegunigalsidase alfa-iwxj Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg administered every 2 weeks (b) (4)	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.	NA		

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.	Lagevrio	62

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: Elfabrio Established name: pegunigalsidase alfa-iwxj Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg administered every 2 weeks (b) (4)	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) ***	60	This name pair has sufficient orthographic and phonetic differences.
2.	(b) (4) ***	59	This name pair has sufficient orthographic and phonetic differences.
3.	(b) (4) ***	58	This name pair has sufficient orthographic and phonetic differences.
4.	(b) (4) ***	56	(b) (4)

No.	Proposed name: Elfabrio Established name: pegunigalsidase alfa-iwxj Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg administered every 2 weeks (b) (4)	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)

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

No.	Name	POCA Score (%)
1.	NA	

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) ***	62	Proposed proprietary name for NDA 216660 found unacceptable by DMEPA (OSE# 2021-1044724277 dated Jan 18, 2022.). Subsequently, the proposed proprietary name Relyvrio*** was found conditionally acceptable for NDA 216660 under OSE # 2022-1044724424 on April 26, 2022.

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.	Filspari***	58

^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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SALI MAHMOUD
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ASHLEIGH V LOWERY
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CHI-MING TU
02/06/2023 11:44:53 AM

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:	February 11, 2021
Application Type and Number:	BLA 761161
Product Name and Strength:	Elfabrio (pegunigalsidase alfa) injection, 20 mg/10 mL (2 mg/mL)
Total Product Strength:	20 mg/10 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Chiesi USA, Inc (Chiesi)
Panorama #:	2020-43995827
DMEPA Safety Evaluator:	Sherly Abraham, R.Ph
DMEPA Team Leader:	Idalia E. Rychlik, Pharm.D.

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Elfabrio, 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. Chiesi submitted an external name study, previously conducted by (b) (4) for this proposed proprietary name. The external study was evaluated in our previous review of the name Elfabrio.^a

1.1 REGULATORY HISTORY

Protalix Ltd, has been actively engaged in co-development of pegunigalsidase alfa injection with the aforementioned Sponsor Chiesi, USA. Protalix, Ltd previously submitted the proposed proprietary name, Elfabrio on July 26, 2019, under IND 110161. However, we found the name, Elfabrio unacceptable due to spelling, orthographic and phonetic similarities, and shared product characteristics with the proprietary name, (b) (4) under IND 110161 on January 15, 2020.^a Hence, Protalix submitted the name, (b) (4) for review on January 25, 2020 under IND 110161 and Chiesi submitted the name, (b) (4) for review on May 27, 2020 under BLA 761161. On July 16, 2020, we found the name, (b) (4) conditionally acceptable under IND 110161 and BLA 761161.^b

During our label and labeling review of BLA 761161, Chiesi noted that their preferred proposed name was Elfabrio for their product. Therefore, we requested Chiesi to withdraw their conditionally accepted name, (b) (4) and resubmit their preferred name, Elfabrio, under BLA 761161.^c Thus, Chiesi withdrew their conditionally approved name, (b) (4) and resubmitted the proposed proprietary name Elfabrio for review on November 19, 2020.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 19, 2020 and prescribing information submitted on May 27, 2020 under BLA 761161.

- Intended Pronunciation: El fa' bree oh
- Nonproprietary Name: pegunigalsidase alfa
- Indication of Use: treatment of adults with a confirmed diagnosis of Fabry disease
- Route of Administration: intravenous

^a Abraham, S. Proprietary Name Review for Elfabrio (IND 110161). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Jan 15. Panorama No. 2019-33427979

^b Abraham, S. Proprietary Name Review for Onabby (IND 110161 and BLA 761161). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 Jul 16. Panorama No. 2020-37412071 (IND) and 2020-40218398 (BLA).

^c Sun, S. Proprietary Name Request Acknowledgement/Withdrawal (BLA 761161). Silver Spring (MD): FDA, CDER, OSE (US); 2020 Nov 9. Panorama No. 2020-40218398.

- Dosage Form: injection
- Strength: 20 mg/10 mL (2 mg/mL)
- Dose and Frequency: 1 mg/kg every other week
- How Supplied: 1, 5, and 10 single use vials 20 mg (10 mL) vials
- Storage: Store vials at 2°C to 8°C (36°F to 46°F). Do not freeze or shake. The product contains no preservative. Diluted solutions should be used immediately. If immediate use is not possible, the diluted solution may be stored for up to 24 hours at 2°C to 8°C (36°F to 46°F) or 8 hours at room temperature.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Elfabrio would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Rare Diseases and Medical Genetics (DRDMG) concurred with the findings of OPDP's assessment for Elfabrio.

2.2 SAFETY ASSESSMENT

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

2.2.1 *United States Adopted Names (USAN) Search*

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

2.2.2 *Components of the Proposed Proprietary Name*

Chiesi did not provide a derivation or intended meaning for the proposed proprietary name, Elfabrio, 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*

In response to the OSE, December 17, 2020 e-mail, the Division of Rare Diseases and Medical Genetics (DRDMG) did not forward any comments or concerns relating to Elfabrio at the initial phase of the review.

^d USAN stem search conducted on January 8, 2021.

2.2.4 FDA Name Simulation Studies

Seventy-five (n=75) practitioners participated in DMEPA's prescription studies for Elfabrio. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^e identified 55 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 four 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. 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 $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	2
Low similarity name pair: combined match percentage score $\leq 54\%$	0

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

Our analysis of the four names contained in Table 1 determined none of the names will pose a risk for confusion with Elfabrio 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 Rare Diseases and Medical Genetics (DRDMG) via e-mail on February 9, 2021. At that time we also requested additional

^e POCA search conducted on January 8, 2021 in version 4.4.

information or concerns that could inform our review. Per e-mail correspondence from the Division of Rare Diseases and Medical Genetics (DRDMG) on February 11, 2021, they stated no additional concerns with the proposed proprietary name, Elfabrio.

3 CONCLUSION

The proposed proprietary name, Elfabrio, is acceptable.

If you have any questions or need clarifications, please contact Su-Lin Sun, OSE project manager, at 301-796-0036.

3.1 COMMENTS TO CHIESI, USA, INC.

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

If any of the proposed product characteristics as stated in your submission, received on November 19, 2020, 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. 6F^f

^f 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 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 names⁹. 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).

⁹ Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

- c. FDA Prescription Simulation Studies: DMEPA 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 $\geq 70\%$).

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?		
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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.

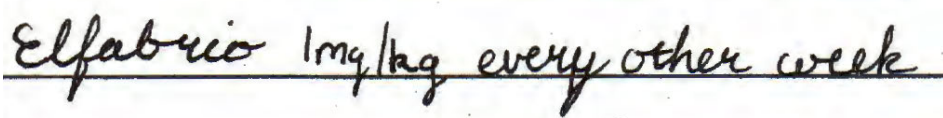
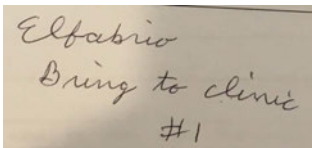
	Orthographic Checklist (Y/N to each question) - Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. - Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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 **≤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. Elfabrio Study (Conducted on January 8, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
<u>Medication Order:</u> 	Elfabrio Bring to clinic #1
<u>Outpatient Prescription:</u> 	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Elfabrio	

FDA Prescription Simulation Responses (Aggregate Report)

209 People Received Study
75 People Responded

Study Name: Elfabrio

Total	26	14	11	24	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
ALFABRIO	0	0	3	0	3
ELFABIO	1	0	0	0	1
ELFABRIA	1	0	0	0	1
ELFABRIO	24	14	6	23	67
ELFABRYO	0	0	1	0	1
ELFRABIO	0	0	0	1	1
OSABRIO	0	0	1	0	1

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

No.	Proposed name: Elfabrio Established name: pegunigalsidase alfa Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg every other week	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.	Elfabrio	100	Proposed proprietary name under review.
2.	(b) (4)	76	(b) (4)

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-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: Elfabrio Established name: pegunigalsidase alfa Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg every other week	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.	Relyvrio***	63	Orthographically, the name pair begins with different first letters (R vs. E) that look different when capitalized. Additionally, the infixes ('yv' vs. 'fab') look sufficiently different. Relyvrio***

No.	Proposed name: Elfabrio Established name: pegunigalsidase alfa Dosage form: injection Strength(s): 20 mg/10 mL (2 mg/mL) Usual Dose: 1 mg/kg every other week	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
			contains the downstroke letter 'y' in the infix and does not contain any upstroke letters whereas Elfabrio contains two upstroke letters 'f' and 'b' in the infix, which gives the infixes different shapes when scripted. Phonetically, the first syllables ('Reh' vs. 'El') and the second syllables ('lee' vs. 'fa') sound different when spoken.

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.	Celadrin	57	International product formerly marketed in Canada, Malaysia and India.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion-N/A

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/

SHERLY ABRAHAM
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SUFFIX REVIEW FOR NONPROPRIETARY NAME

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:	October 20, 2020
Responsible OND Division:	Division of Rare Diseases and Medical Genetics (DRDMG)
Application Type and Number:	BLA 761161
Product Name and Strength:	(b) (4) (pegunigalsidase alfa-iwxj) injection, 20 mg/10 mL (2 mg/mL)
Product Type:	Single Ingredient Product
Applicant/Sponsor Name:	Chiesi USA (Chiesi)
OSE RCM #:	2020-1625
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy 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 761161.

1.1 Regulatory History

Chiesi 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

pegunigalsidase alfa-iwxj

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

We determined that the FDA-generated suffix -iwxj, 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'S ANALYSIS

These findings were shared with OPDP. In email correspondence dated October 15, 2020, OPDP did not identify any concerns that would render this suffix unacceptable. DMEPA also communicated our findings to the Division of Rare Diseases and Medical Genetics (DRDMG) via e-mail on October 20, 2020.

^a Harris, D. General Advice Letter for BLA 761161. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US) 2020 Aug 11.

^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 -iwxj acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to pegunigalsidase alfa-iwxj. DMEPA will communicate our findings to the Applicant via letter.

4.1 Recommendation for Chiesi USA

We find the nonproprietary name, pegunigalsidase alfa-iwxj, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, pegunigalsidase alfa-iwxj 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.

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/s/

CARLOS M MENA-GRILLASCA
10/20/2020 11:41:08 AM

DANIELLE M HARRIS
10/21/2020 02:48:26 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:	July 16, 2020
Application Type and Number:	IND 110161 and BLA 761161
Product Name and Strength:	(b) (4) (pegunigalsidase alfa) injection 20 mg/10 mL (2 mg/mL)
Total Product Strength:	20 mg/10 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Protalix Limited (Protalix) and Chiesi USA, Inc (Chiesi) ^a
Panorama #:	2020-37412071 (IND) 2020-40218398 (BLA)
DMEPA Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA Team Leader:	Idalia E. Rychlik, Pharm.D.

^a The Sponsor of IND 110161, Protalix Ltd, is actively engaged in co-development with Chiesi on the original BLA 761161.

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SHERLY ABRAHAM
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