CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Memo for Proprietary Name- Vimizim

Date:	1/13/14
Reviewer:	Lubna Merchant, M.S., PharmD, Team Leader Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Vimizim (Elosulfase alfa) Injection, 1 mg/mL
Application Type/Number:	BLA 125460
Sponsor:	Biomarin

*** This document contains proprietary and confidential information that should not be released to the public.***

DMEPA found the proposed name, Vimizim, acceptable in OSE Review # 2013-1045 dated July 24, 2013. In this review we indicated the proposed proprietary name must be re-reviewed prior to approval of the BLA. However, DMEPA no longer re-reviews proposed proprietary names within 90 days of the anticipated application approval, unless there is a change in the proposed product characteristics.

Since none of the proposed product characteristics were altered, our conclusion that the proposed proprietary name is acceptable has not changed since the aforementioned review. DMEPA has no objection to the proprietary name, Vimizim, for this product at this time.

If you have further questions or need clarifications, please contact Phong Do, OSE project manager, at 301-796-4795.

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/s/

LUBNA A MERCHANT
01/13/2014

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	July, 24 2013
Reviewer:	Denise V. Baugh, PharmD, BCPS Division of Medication Error Prevention and Analysis
Team Leader:	Lubna Merchant, PharmD, M.S. Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Vimizim (Elosulfase alfa) Injection, 1 mg/mL
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OSE RCM #:	2013-1045

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Vimizim, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 PRODUCT INFORMATION

Vimizim was reviewed under IND 101234 and found acceptable (OSE Review# 2012-1274 dated November 6, 2012). The product characteristics have changed since the IND review. See Table 1 below for details.

The following product information is provided in the May 1, 2013 proprietary name submission and includes changes to the product characteristics:

Table 1. Product Characteristics for Vimizim – May 1, 2013 Submission

	IND 101234	BLA 125460
Active Ingredient	galactosamine (N-acetyl)-6-sulfate sulfatase'	elosulfase alfa
Dosage form	Solution for injection	Solution for Infusion
Indication of Use	enzyme replacement therapy for all MPS IVA (Morquio) patients	enzyme replacement therapy for all MPS IVA (Morquio) patients
Route of Administration	intravenous infusion	intravenous infusion
Strength*	(b) (4)	1 mg/mL
Dose	2 mg/kg	2 mg/kg
Frequency of Administration*	once weekly (b) (4)	once weekly
How Supplied	single dose pack (vials)	single dose pack (vials)
Storage	Refrigerated	Refrigerated
Container closure system	Vial: clear, tubing glass; Stopper: (b) (4) rubber; (b) (4) seal: aluminum flip-off overseal	Vial: clear, tubing glass; Stopper: (b) (4) rubber; (b) (4) seal: aluminum flip-off overseal
Additional information	Product is to be given by a healthcare professional in an infusion clinic; specialty pharmacy will dispense product	Product is to be given by a healthcare professional in an infusion clinic; specialty pharmacy will dispense product

*

* Product characteristics which have changed.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Gastroenterology and Inborn Errors Products (DGIEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

The June 23, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Vimizim, has no intended meaning or derivation. 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 FDA Name Simulation Studies

Twenty-five practitioners participated in DMEPA's prescription studies. Although there were no interpretations that overlapped with any currently marketed products, two participants (one each in the inpatient and outpatient study) commented that the proprietary name looked like two currently marketed names: Viagra ("especially when scripted in cursive") and Vimovo ("Too similar to Vimovo"). We added the name Viagra to our list of potentially similar names and the name Vimovo was previously identified but re-evaluated because of the change in product characteristics. The remaining interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. The most frequent misinterpretations were the erroneous interpretation of the letter 'V' for 'Y' or 'Z' and the misinterpretation of the second 'm' for 'n'. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results of the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, May 29, 2013 e-mail, the Division of Gastroenterology and Inborn Errors Products (DGIEP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists the possible orthographic and phonetic misinterpretations of the letters considered when searching for names with similar appearance and sound to the proposed proprietary name, Vimizim. Since the product characteristics have changed, we re-reviewed the previous names thought to be potentially similar to Vimizim listed in OSE RCM #2012-1274 and confirmed the change in product characteristics has not altered our previous conclusion regarding the acceptability of the proposed proprietary name. Table 1 lists the additional names identified to have similar orthographic, phonetic, or spelling similarity to the proposed proprietary name, Vimizim since our last review.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines and Prescription Studies)

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Minocin	FDA	Risamine	FDA	Viagra	Rx Study Participant
(b) (4)	FDA	(b) (4)	FDA	(b) (4)	FDA
Nimbex	FDA	Vimax	FDA	Lumigan	FDA
Vusion	FDA	Ningxia	FDA	Vimovo	Prescription Simulation Study
Yasmin	FDA				
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Elosulfase alfa	FDA	Lumizyme	FDA		

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Our analysis of the fifteen names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined fifteen names will not pose a risk for confusion as described in Appendices D through E.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Gastroenterology and Inborn Errors Products (DGIEP) via e-mail on July 2, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Gastroenterology and Inborn Errors Products (DGIEP) on July 8, 2013, they stated their concern that the prefix 'vim' may indicate that this drug product denoted "vigor, vitality, and energy" and was therefore promotional. After a joint, internal meeting between DGIEP, DMEPA, and OPDP on July 18, 2013, the Division's concerns were minimized and they aligned with OPDP's decision regarding the proprietary name, Vimizim.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Phong Do, OSE Project Manager, at 301-796-4795.

3.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name must be re-reviewed 90 days prior to approval of the BLA. The results are subject to change. If any of the proposed product characteristics as stated in your May 1, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

1. ***Micromedex Integrated Index (http://csi.micromedex.com)***

   Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

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

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)***

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

   DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. ***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.

6. ***Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)***

   Drugs@FDA contains most of the drug products approved 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. ***U.S. Patent and Trademark Office (http://www.uspto.gov)***

   USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)***

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. ***Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)***

   The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

10. ***Natural Medicines Comprehensive Databases (www.naturaldatabase.com)***

    Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

11. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

13. ***Red Book (www.thomsonhc.com/home/dispatch)***

    Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

14. ***Lexi-Comp (www.lexi.com)***

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

15. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

16. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

18. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. ***Dogpile (www.dogpile.com)***

    Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

20. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). 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. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

Three 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 or verbal pronunciation of the drug name. 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 orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. 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.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[3] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

[3] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

Moreover, DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Vimizim	Scripted May Appear as	Spoken May Be Interpreted as
V	Y, Z, U, C, M, L, N, R	F, B, Z
v	n, r, u, w	b, f
i	e, l	y, e
m	rn, nn, n, v, w, wi, vi, onc, z	n
z	c, e, g, n, m, q, r, s, v	s, c
Letter Strings		
vim	vis, yim	zim
zim	zin, zion, ism, ium	zin, zen, sin, zine
iz	n	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Vimizim Study (Conducted on June 15, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Vimizim 140 mg intravenous today x 1 dose. Outpatient Prescription: Vimizim #1 vial Bring to clinic	"Vimizim, Dispense 1 vial - bring to clinic"

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
?	0	1	0	1
VIMAZIM	0	1	0	1
VIMI ZION	0	0	1	1
VIMIZIM	1	1	6	8
VIMIZIN	0	2	1	3
VIMOZEN	0	1	0	1
VISPRISM	0	0	1	1
YIMIUM	1	0	0	1
YIMIZIM	5	0	0	5
ZIMASIN	0	1	0	1
ZIMAZIN	0	1	0	1
ZIMAZINE	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Vimizim	Failure preventions
1.	Elosulfase alfa	Active ingredient for the proprietary name, Vimizim	Look and Sound Alike	Same product characteristics as the proprietary name Vimizim and therefore confusion is not expected to occur.
2.	Vimax	Sildenafil	Look Alike	International product marketed in Indonesia
3.	Ningxia	Herbal product also known as "Lycium"	Look Alike	Name was identified in Natural Medicines Database, but product characteristics were not found in other commonly used drug databases.
4.	(b) (4)	No USAN established name	Look alike	(b) (4) is the alternate, proposed proprietary name to (b) (4) which DMEPA found to be acceptable (OSE Review 2012-671 dated July 25, 2012).
5.	(b) (4)	Itraconazole	Look alike	(b) (4) is the alternate, proposed proprietary name for Onmel. NDA 22484 was approved April 28, 2010 with the proprietary name, Onmel

*** This document contains proprietary and confidential information that should not be released to the public.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

No.	**Proposed name: Vimizim** **Dosage Form(s): Injection** **Strength(s): 1 mg/mL** **Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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.	Minocin (minocycline) Capsule 50 mg and 100 mg Injection 100 mg/vial *Usual dose*: 100 mg orally or intravenously every 12 hours (not to exceed 400 mg per day) or 50 mg four times daily;	Orthographic similarity stems from the similar appearance of their first , third and seventh letters ('M' vs. 'V' and 'n' vs. 'm') in some handwriting samples and the fact that both names share the letter 'i' in the 2nd and 6th positions. Additionally, both names are the same length (7 letters). A potentially similar product characteristic includes the dose (100 mg). Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product	The marketed name, Minocin, includes the infix 'no' which may look different from the letters 'mi' in the infix of the proposed name, Vimizim when written. Differing product characteristic may include the frequency of administration (every 12 hours vs. once weekly). .

No.	Proposed name: Vimizim Dosage Form(s): Injection Strength(s): 1 mg/mL Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
2.	Risamine (Menthol and Zinc Oxide) Ointment 0.44%/20.625% (113 grams) *Usual dose*: Apply thin layer to clean, dry skin 2 to 4 times daily or after each incontinent episode/diaper change	Orthographic similarity stems from the similar appearance of their 1st and 7th letters ('R' vs. 'V' and 'n' vs. 'm') in some handwriting samples and the fact that they share the same letter in the 2nd and 6th positions ('i'). Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product	The marketed name, Risamine, includes the letter string 'sa' in the 3rd and 4th positions which looks different from the letter string 'mi' (in Vimizim) when scripted. This is because the letter 'm' is wider in structure than the letters's' or 'a'. Additionally, the name Risamine appears longer in length when scripted. Differing product characteristics include the dose ('thin' layer vs. 2 mg/kg) and the frequency of administration (2 to 4 times daily vs. once weekly).

No.	Proposed name: Vimizim Dosage Form(s): Injection Strength(s): 1 mg/mL Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
3.	(b) (4)* (Drospirenone and Ethinyl Estradiol) Tablets 0.3 mg/0.02 mg *Usual dose*: One tablet orally daily	Orthographic similarity stems from sharing the first 3 letters in their names ('Vim'). Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product	The pending proprietary name, Vimya***, includes a down stroke ('y') which gives this name a different shape from that of the proprietary name, Vimizim (assuming the letter 'z' is not scripted as a down stroke). Additionally, Vimizim is longer in length than Vimya*** when scripted (5 letters vs. 7 letters). Differing product characteristics include the dose (one tablet vs. 2 mg/kg) and the frequency of administration (once daily vs. once weekly).

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No.	Proposed name: Vimizim Dosage Form(s): Injection Strength(s): 1 mg/mL Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
4.	Nimbex (Cisatracurium) Injection 2 mg and 10 mg *Usual dose*: Dose is individualized; following an initial dose of 0.15 mg/kg to 0.2 mg/kg, a dose of 0.03 mg/kg is recommended for maintenance of neuromuscular blocking action during prolonged surgical procedures	Orthographic similarity stems from the similar appearance of their first letters ('N' vs. 'V') and the fact that both names share their 2nd and 3rd letters ('im'). There is numerical similarity in dose (0.2 mg/kg vs. 2 mg/kg).	The marketed name, Nimbex, includes an up stroke ('b') and a cross stroke ('x') which gives this name a different shape from that of the proposed name, Vimizim. The settings of use for these drug products differ and will likely minimize the risk of confusion between this name pair. Nimbex is likely to be stored and used in practice settings where surgical procedures occur and therefore, is not likely to be confused with the proposed name, Vimizim.
5.	Lumigan (Bimatoprost) Ophthalmic Solution 0.01 % and 0.03 % *Usual dose*: One drop in the affected eye(s) each evening	Orthographic similarity stems from the similar appearance of their 1st and 7th letters ('L' vs. 'V' and 'n' vs. 'm') in some handwriting styles and the fact that both names share the same letters in the 3rd and 4th positions ('m' and 'i'). There is also a potential similarity in shape if the letter 'z' is written as a down stroke in Vimizim. Additionally, both names are identical in length (7 letters).	Differing product characteristics include the dose (one drop vs. 2 mg/kg) and the frequency of administration (each evening vs. once weekly). Since Lumigan is available in more than one strength, this information is needed on a prescription or medication order to dispense/administer the medication as intended. There is no overlap or similarity in strengths.

No.	**Proposed name: Vimizim** **Dosage Form(s): Injection** **Strength(s): 1 mg/mL** **Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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**
6.	Vusion (Miconazole Nitrate, White Petrolatum, and Zinc Oxide) Ointment 0.25%/81.35%/15% *Usual dose*: Apply thin later to the affected area at each diaper change for 7 days	Orthographic similarity stems from sharing their 1st and 4th letters ('V' and 'i') and the fact that their last letters may look similar when scripted ('n' vs. 'm'). Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product	Differing product characteristics include the dose ('thin' layer vs. 2 mg/kg) and the frequency of administration (at each diaper change vs. once weekly).

No.	**Proposed name: Vimizim** **Dosage Form(s): Injection** **Strength(s): 1 mg/mL** **Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**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**
7.	Lumizyme (Alglucosidase alfa) for Injection 5 mg/mL <u>*Usual dose*</u>: 20 mg/kg by intravenous infusion every 2 weeks	Orthographic similarity stems from the similar appearance of their first letters ('L' vs. 'V') in some handwriting styles. Additionally, both names share the letter 'm' in the 3rd and 7th positions. Overlapping product characteristics include the route of administration (intravenous infusion) and the frequency of administration (on a weekly basis - once weekly vs. every 2 weeks). Numerical similarity in dose exists (20 mg/kg vs. 2 mg/kg) Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product.	The marketed name, Lumizyme, includes at least one down stroke ('y') - if you do not script the letter 'z' as a down stroke. This feature gives this name a different shape from the proposed name, Vimizim. Additionally, the letter 'u' in the 2nd position within Lumizyme is wider in structure than the letter 'i' in the 2nd position within the name, Vimizim. Finally, the terminal letter 'e' (in Lumizyme) gives this name a longer appearance when scripted.

No.	Proposed name: Vimizim Dosage Form(s): Injection Strength(s): 1 mg/mL Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	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
8.	Viagra (Sildenafil) Tablet 25 mg, 50 mg, 100 mg *Usual dose*: 25 mg to 100 mg as a single dose taken 30 minutes to 4 hours before sexual activity	Orthographic similarity stems from sharing the first 2 letters of their name ('Vi'). Potential overlapping product characteristic is the dose (100 mg).	The marketed name, Viagra, includes a single down stroke ('g') in its name which gives it a different shape from that of the proposed proprietary name, Vimizim (assuming the letter 'z' is not scripted as a down stroke). Additionally, the letter string 'im' appears twice in the name, Vimizim, giving it a repetitive characteristic and a longer length and this may distinguish this name from the name, Viagra. One differing product characteristic is the frequency of administration (single dose vs. once weekly).
9.	Vimovo (Naproxen and Esomeprazole) Delayed-release Tablets 375 mg/20 mg, 500 mg/20 mg *Usual dose*: One tablet twice daily taken at least 30 minutes before meals	Orthographic similarity stems from sharing the first 3 letters in their names (Vim-).	The last three letters of the marketed name, Vimovo (ovo), differ orthographically from the last four letters in Vimizim (izim). This difference also makes the name, Vimizim appear longer when written. Differing product characteristics include strength (375 mg/20 mg, 500 mg/20 mg vs. 1 mg/mL), dose (one tablet vs. 2 mg/kg), and frequency of administration (twice daily vs. once weekly). A prescription for the marketed name, Vimovo requires a strength (375 mg/20 mg or 500 mg/20 mg) in order to be dispensed/administered. vs. Vimizim which is available in a single strength and therefore this information does not have to be written on the prescription to dispense/administer the product..

No.	**Proposed name: Vimizim** **Dosage Form(s): Injection** **Strength(s): 1 mg/mL** **Usual Dose: 2 mg/kg given intravenously over 4 hours once weekly**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
10.	Yasmin (drospirenon and ethinyl estradiol) Tablets 3 mg/0.03 mg *Usual dose*: One tablet orally daily	Orthographic similarity stems from the similar appearance of their first letters ('Y' vs. 'V') in some handwriting styles and the fact that their last 2 letters are identical or similar when written ('in' vs. 'im'). Both drug products are available in one strength and therefore this information is not needed on a medication order/prescription prior to dispensing/administering either drug product	The letters in the 2nd through 4th positions in the marketed name Yasmin and the proposed name, Vimizim do not look similar when written ('asm' vs. 'imi'). Differing product characteristics include the dose (one tablet vs. 2 mg/kg) and the frequency of administration (once daily vs. once weekly).

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/s/

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