CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-575

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

Date:	December 9, 2009
To:	Donna Griebel, MD, Director Division of Gastroenterology Products
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Deveonne Hamilton-Stokes, RN, BSN, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Vpriv (Velaglucerase alfa) for Injection 200 units/vial and 400 units/vial
Application Type/Number:	NDA 022575
Applicant:	Shire Human Genetic Therapies, Inc.
OSE RCM #:	2009-1760

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

CONTENTS

EXECUTIVE SUMMARY

Vpriv is the proposed proprietary name for Velaglucerase alfa for Injection. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Vpriv conditionally acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Shire Human Genetic Therapies, Inc., dated September 22, 2009, for an assessment of the proposed proprietary name, Vpriv, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted an external evaluation of the proposed proprietary name conducted by ——. Container labels, carton labeling and insert labeling were also submitted, but will be reviewed under separate cover. b(4)

1.2 PRODUCT INFORMATION

Vpriv (Velaglucerase alfa) for Injection is indicated for long-term enzyme replacement therapy for pediatric and adult patients with type 1 Gaucher disease. The usual recommended dose is 60 U/kg administered every other week as a 60-minute intravenous infusion. Vpriv will be available as 200 unit and a 400 unit vial and should be stored in a refrigerator at 2° to 8° C (36° to 46° F).

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Vpriv.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'V' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[1,2]

To identify drug names that may look similar to Vpriv, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (five letters), upstrokes (1, capital letter 'V'), down strokes (one, lower case letter 'p'), cross strokes (none), and

---

[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[2] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

dotted letters (one, lower case letter 'i'). Additionally, several letters in Vpriv may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Vpriv.

When searching to identify potential names that may sound similar to Vpriv, the DMEPA staff search for names with similar number of syllables (two), stresses (VEE priv or vee PRIV), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'V' may sound like 'Z' and 'priv' may sound like 'prive' and 'prev'. (See Appendix B). The Applicant's intended pronunciation (VEE-priv) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following medication orders and outpatient and verbal prescriptions were communicated during the FDA prescription studies.

Figure 1. Vpriv Rx Study (conducted on October 9, 2009)

HANDWRITTEN OUTPATIENT PRECRIPTIONS	VERBAL RESCRIPTION
Inpatient Order: Vpriv 4200 units IV	"Vpriv 200 units Dispense #1 Use as directed"
Outpatient Prescription : Vpriv 200 units IV	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an independent risk assessment of the proposed proprietary name conducted by a consulting firm, The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in the Division of Medication Error Prevention and Analysis staff's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing names could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether DMEPA's risk assessment concurs or differs with the findings of the external risk assessment. When the proprietary name risk assessments differ, we provide a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 13 names as having some similarity to the name Vpriv.

Nine of the names were thought to look like Vpriv. These include: Vopac, Zyprexa Relprev***, Verv, Vitec, Sprix***, Vesprin, Viper, Lupron and Vibativ. The two names thought to sound like Vpriv are Bepreve and Vepesid. The remaining names (Vfend and VIGIV) were thought to look and sound similar to Vpriv.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of November 12, 2009.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Vpriv.

DDMAC had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 21 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 9% of the participants (n=2) interpreted the name correctly as "Vpriv", with correct interpretation occurring in the verbal study. The remainder of the respondents (n=19) misinterpreted the drug name. In the inpatient medication order study all of the respondents misinterpreted the beginning letter of the name 'V' as the letter 'U'. In the outpatient prescription study the capital letter 'V' was misinterpreted as the letter 'U' and the ending letter 'v' was misinterpreted as the letter 'o'. In the verbal prescription study the capital letter 'V' was misinterpreted as the letter 'Z' and the ending letter 'v' was misinterpreted as the letter 'z'. Additionally, respondents in the voice and outpatient prescription studies interpreted the name as 'V-Priv' (4 respondents) and 'V priv' (1), respectively. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME ASSESSMENT

In the proposed name risk assessment submitted by the Applicant — identified a total of 5 drug names as having some potential for confusion with the name Vpriv.

Of the 5 names, DMEPA identified the following 2 names during the database searches: Vepesid and Vfend. The remaining 3 names (Cipro, Epivir and Versed) were evaluated as part of the safety evaluator risk assessment.

3.5 COMMENTS FROM THE DIVISION

In response to the OSE email dated October 8, 2009, the Division of Gastroenterology Products did not forward any comments and/or clinical/other concerns on the proposed name at the initial phase of the name review.

On November 18, 2009, DMEPA notified the Division of Gastroenterology Products via e-mail that we had no objections to the proposed proprietary name, Vpriv. Per e-mail correspondence from the Division of Gastroenterology Products on December 1, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Vpriv.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified five additional names (Valpin 50, Virac Rex, Vira-a, Zipsor and Z pak) which were thought to look or sound similar to Vpriv and represent a potential source of drug name confusion.

4 DISCUSSION

DDMAC and the Review Division had no concerns with the proposed proprietary name, Vpriv.

DMEPA identified and evaluated 21 names for their potential similarity to the proposed name, Vpriv. Two names lacked orthographic and/or phonetic similarity to Vpriv, one name had limited information in commonly used drug references, one name was never marketed and four names are no longer marketed and have no generics available (see Appendices D through G). Thus, these names were eliminated from further evaluation.

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 13 names and lead to medication errors. This analysis determined that the name similarity between Vpriv and these 13 products was unlikely to result in medication errors for the reasons presented in Appendices H through J. Additionally, DMEPA did not identify any other factors that would render the name acceptable at this time. This finding is consistent with the independent name study.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Vpriv, is not vulnerable to name confusion that could lead to medication errors nor was it considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Vpriv, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. The proposed name must be re-reviewed 90 days before approval of the NDA. For questions or clarifications, please contact Nina Ton, OSE Project Manager, at 301-796-1648.

5.1 COMMENTS TO THE APPLICANT

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

Vpriv will be re-reviewed 90 days prior to approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

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.

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in 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. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

USPTO provides information regarding patent and trademarks.

9. 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.

10. 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.

11. 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.

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

15. Lexi-Comp (www.lexi.com)

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. 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. [3]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment 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 focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the

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

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

proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. 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.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug 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.

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. Because drug name confusion can occur at any point in the medication use process, DMEPA staff 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.[5] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such 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). In addition, the DMEPA staff 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. 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.

[5] 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 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, the DMEPA staff also 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 staff conducts searches of 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 using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use 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, the DMEPA staff review 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.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). 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 DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of 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 Analysis 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 the 123 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 send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and 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 DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or 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 concur/not concur with DMEPA's final decision.

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, conducts a Failure Mode and Effects Analysis, and provides an overall 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.[6] 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 characteristics listed in Section one. 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?"***

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. 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.

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 Risk Assessment:

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC'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)].

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

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.

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 is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to 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 Sponsor. However, the safety concerns set forth in criteria a through e 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 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 a 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. . (See Section 4 for limitations of the process).

Appendix B: Potential orthographic or phonetic misinterpretations of the letters in Vpriv

Letters in Name, Vpriv	Scripted may appear as	Spoken may be interpreted as
Capital 'V'	L, U, Z	F, Z
lower case 'p'	s	-
lower case 'r'	c, n, v	wr
lower case 'i'	c, e, l	any vowel
lower case 'v'	o, r, u	z

Appendix C:

CDER Prescription Study Responses

Inpatient Medication Order	Voice Prescription	Outpatient Prescription
Upriv	V-Priv	Upriv
Upriv	Zpriv	Uprio
Upriv	V-Priv	Upriv
Upriv	Zepriz	V priv
Upriv	V-Priv	Upriv
Upriv	Vpriv	
Upriv	Veepriv	
	Vpriv	
	V-Priv	

Appendix D: Names without convincing look-alike and/or sound-alike similarities to Vpriv

Proprietary Name	Similarity to Vpriv
Zyprexa Relprev***	Look
Versed	Look and/or Sound

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

Appendix E: Product with limited or no additional information found in DMEPA References 1-16 (pages 7 and 8)

Proprietary Name	Similarity to Vpriv	Additional Information
Verv	Look	Caffeine is active ingredient; over the counter product no longer available per revolutionhealth.com

Appendix F: Product never marketed

Proprietary Name	Similarity to Vpriv	Additional Information
Vigiv	Look and Sound	Vigiv is the abbreviation for Vaccinia Immune Globulin Intravenous. Per CBER, the product was revoked and never marketed. Product was contracted by DoD and thus would not have been on the market for general sales.

Appendix G: Drug products that are discontinued and no generic equivalent is available

Proprietary Name (Active Ingredient)	Similarity to Vpriv	Status
Vesprin (Triflupromazine Hydrochloride)	Look	Discontinued per Orange Book and product not found in 2009 Redbook
Valpin 50 (Anisotropine Methylbromide)	Look and Sound	Discontinued per Orange Book and product not found in 2009 Redbook
Virac Rex (Undecoylium Chloride and Undecoylium Chloride iodine complex)	Look	Discontinued per Orange Book and product not found in 2009 Redbook
Vira-a (Anisotropine Methylbromide)	Look	Discontinued per Orange Book and product not found in 2009 Redbook

Appendix H: Products with no numerical overlap in strength or usual dosage.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Dosage Form/Strength	Usual Dosage Recommendations
Vpriv (Velaglucerase alfa)	**NA**	**Injection: 200 units/vial, 400 units/vial**	**60 units/kg intravenously administered every other week as a 60 minute intravenous infusion**
Sprix*** (Ketorolac tromethamine)	Look	Nasal Spray: 15.75 mg	One 15.75 mg spray in each nostril every 6 to 8 hours OR For special populations: One 15.75 mg spray in only one nostril every 6 to 8 hours for up to 5 days
Vopac (Codeine/Acetaminophen)	Look	Tablet: 30 mg/650 mg	½ to 2 tablets every 4 hours
Vitec (Vitamin E) (OTC)	Look	Cream	Apply a thin layer to affected area as needed for sunburn, diaper rash, dry skin
Viper (Unique blend of natural herbs) (OTC)	Look	Capsule	Take 2 capsules one to two times daily
Vibativ (Telavancin Hydrochloride)	Look	Injection: 250 mg, 750 mg	10 mg/kg administered over 60 minutes by intravenous infusion once every 24 hours for 7 to 14 days
Bepreve (Bepotastine Besilate)	Sound	Ophthalmic solution: 1.5%	Instill 1 drop into the affected eye(s) twice a day
Zipsor (Diclofenac potassium)	Look	Capsule: 25 mg	25 mg by mouth four times a day
Epivir (Lamivudine)	Look	Tablet: 150 mg, 300 mg Oral Solution: 10 mg/mL	Tablet: 300 mg daily by mouth administered as either 150 mg twice daily or 300 mg once daily Oral solution: 4 mg/kg twice daily
Zpak* (Brand name is Zithromax Zpak) (Azithromycin)	Look	Tablets: 250 mg	Two 250 mg tablets on the first day and one 250 mg tablet once daily for the next 4 days

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

Appendix I: Potential confusing names with numerical overlap in strength or dose; however, risk of confusion with Vpriv minimized because of other differentiating product characteristics and orthographic differences

Failure Mode: Name Confusion	**Causes (could be multiple)**	**Rationale why medication errors are unlikely to occur in the usual practice setting**
Vpriv **(Velaglucerase alfa)** **Injection: 200 units/vial, 400 units/vial**		**60 units/kg intravenously administered every other week as a 60 minute intravenous infusion**
Vfend (Voriconazole) Suspension, Tablet, Injection: 200 mg Usual dose: *Loading dose:* Intravenous 6 mg/kg every 12 hours for the first 24 hours *Maintenance dose:* Intravenous range of 3 mg/kg to 4 mg/kg every 12 hours Oral dose 200 mg every 12 hours	Orthographic similarity: Both begin with the letter 'V'; middle letters 'pr' vs. 'fe' may look similar Phonetic similarity: Both are 2 syllables; identical first syllable /v/ Overlapping numerical portion of strength: 200 Same route of administration: intravenously	Although Vpriv and Vfend share an overlapping numerical portion of their strength, differentiating product characteristics as well as orthographic and phonetic differences in the name will help reduce the risk of medication errors. The product endings help to provide orthographic differentiation 'iv' vs. 'nd' and the second syllables /priv/ vs. /fend/ help to provide phonetic distinction. Additionally, the products have differentiating characteristics such as frequency of administration (every other week vs. every 12 hours) and unit of measurement (units vs. mg). Lastly, Vpriv must be stored in the refrigerator.
Cipro (Ciprofloxacin) Suspension: 250 mg/5 mL, 500 mg/5 mL Injection: 200 mg/20 mL, 400 mg/40 mL Tablet: 100 mg, 250 mg, 500 mg, 750 mg Usual dose: 200 mg to 400 mg every 8 to 12 hours for 7 days to 6 weeks depending on condition being treated	Orthographic similarity: Both share middle letters 'pr' in similar positions, ending letter 'v' vs. 'o' may look similar when scripted Overlapping numerical portion of strength: 200 Overlapping route of administration: intravenously	Although Vpriv and Cipro share an overlapping numerical portion of their strength, differentiating product characteristics as well as orthographic differences in the name will help reduce the risk of medication errors. The beginning letters 'V' vs. 'C' may help provide distinction. Additionally, the products have differentiating characteristics such as frequency of administration (every other week vs. every 8 to 12 hours), unit of measurement (units vs. mg) and usual dose (60 units/kg vs. 200 mg to 400 mg). Lastly, because Cipro is an antibiotic a duration of therapy may be included on an order.

Failure Mode: Name Confusion	Causes (could be multiple)	Rationale why medication errors are unlikely to occur in the usual practice setting
Vpriv **(Velaglucerase alfa)** **Injection: 200 units/vial, 400 units/vial**		**60 units/kg intravenously administered every other week as a 60 minute intravenous infusion**
Vepesid (Etoposide) Injection : 20 mg/mL Testicular cancer: 50 mg/m^2 to 100 mg/m^2/day on days 1 through 5 to 100 mg/m^2/day on days 1, 3, 5 Small Cell Lung Cancer: 35 mg/m^2/day for 4 days to 50 mg/m^2/day for 5 days	Orthographic similarity: Both share similar beginnings 'Vp' vs. 'Vep' Numerically similar numerical portion of strength: 60 vs. 50 Overlapping route of administration: intravenously	Although the numerical portion of the strength of Vpriv and Vepesid are similar, orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. The endings letters 'riv' in Vpriv look orthographically different from the ending letters 'esid' in Vepesid and thus should help to provide differentiation. Additionally, Vpriv contains 5 letters compared to the 7 letters in Vepesid and appears shorter when scripted. The products have differentiating product characteristics such as frequency of administration (every other week vs. once daily up to 5 days), unit of measurement (units vs. mg) and usual dose (60 units/kg vs. 35 mg/m^2/day to 100 mg/m^2/day). Also, due to the fact that the dosing would be individualized for each patient, the numerically similar strength (60 vs. 50) would not cause confusion, since the products will not likely be ordered by the strength.
Lupron (Leuprolide Acetate Injection: 1 mg/0.2 mL 50 mcg/kg/day administered as a single subcutaneous injection	Orthographic similarity: Both share the letters 'pr' in similar positions and beginning letter 'V' vs. 'L' may look similar when scripted Numerically similar numerical portion of strength: 60 vs. 50 Overlapping dosage form: Injection	Although the numerical portion of the strength of Vpriv and Lupron are similar, orthographic differences in the name as well as differentiating product characteristics will help reduce the risk of medication errors. The endings letters 'iv' in Vpriv look orthographically different from the ending letters 'on' in Lupron and thus should help to provide differentiation. The products have differentiating product characteristics such as route of administration (subcutaneous vs. intravenous infusion) frequency of administration (every other week vs. daily), unit of measurement (units vs. mcg) and usual dose (60 units/kg vs. 50 mcg/kg/day). Also, due to the fact that the dosing would be individualized for each patient, the numerically similar strength (60 vs. 50) would not cause confusion, since the products will not likely be ordered by the strength. Lastly, Vpriv must be stored in the refrigerator.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22575	ORIG-1	SHIRE HUMAN GENETIC THERAPIES INC	VELAGLUCERASE ALFA

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DEVEONNE G HAMILTON-STOKES
12/09/2009

DENISE P TOYER
12/10/2009

CAROL A HOLQUIST
12/10/2009