CENTER FOR DRUG EVALUATION AND RESEARCH

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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

Proprietary Name Review

Date:	October 11, 2011
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Drug Name(s):	Voraxaze (Glucarpidase) Injection 1000 units/vial
Application Type/Number:	BLA 125327
Submission Number:	0007
Applicant/sponsor:	BTG International, Inc.
OSE RCM #:	2011-2548

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

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Voraxaze for Glucarpidase Powder for Injection, 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 REGULATORY HISTORY

This review responds to a request from BTG International Inc., dated July 18, 2011, for a safety and promotional assessment of the proposed proprietary name, Voraxaze (BLA 125327). Additionally, the Applicant submitted container labels, carton, and Prescribing Information labeling on June 30, 2011, which will be reviewed separately in OSE review # 2011-2549. The proprietary name, Voraxaze was submitted to the FDA under IND 011557 on May 16, 2006. DMEPA found the name, Voraxaze acceptable in OSE Review #06-0178, dated July 31, 2006.

1.2 PRODUCT INFORMATION

Voraxaze (Glucarpidase) is indicated for the (b) (4) reduction of toxic Methotrexate concentration due to impaired renal function. The recommended dose of Voraxaze is a single intravenous injection of 50 Units per kilogram of body weight (b) (4) Voraxaze should be administered intravenously over 5 minutes as a bolus injection. Voraxaze is available as lyophilized powder in 3 mL single use vials containing 1000 Units of Glucarpidase. The powder should be reconstituted with 1 mL of sterile normal saline solution. Reconstituted Voraxaze should be used immediately (b) (4) (b) (4)

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Biologic Oncology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on July 28, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

This name is comprised of a single word that does not contain components (e.g. route of administration, dosage form, etc.) that can contribute to medication error or render the name unacceptable

2.2.3 FDA Name Simulation Studies

Twenty-two practitioners participated in DMEPA's prescription studies. None of the responses overlapped with a currently marketed product. Five participants interpreted the proposed proprietary name correctly as 'Voraxaze', with all the correct interpretations (n=5) occurring with outpatient orders. Most of the misinterpretations occurred with the letter 'z'. Seven participants (n=7) in the inpatient studies misinterpreted letter 'z' as letter 'r', two participants (n=2) in the voice studies misinterpreted letter 'z' as letter 's', and one participant (n=1) in the outpatient studies misinterpreted letter 'z' as letter 'y'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, July 28, 2011 e-mail, the Division of Biologic Oncology Products (DBOP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Voraxaze. These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

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

Look Similar	
Name	***Source***
Vorozole	EPD Panel
Veramyst	EPD Panel
Vasoxyl	EPD Panel
Voreloxin	EPD Panel
Veregen	EPD Panel
Vesicare	EPD Panel
Noroxin	EPD Panel

Versaclear	EPD Panel
Norvasc	EPD Panel
Vancenase	EPD Panel
Vancocin	EPD Panel
Voltaren	EPD Panel
Voriconazole	EPD Panel
Solaraze	EPD Panel
Abraxane	EPD Panel
Voluven	EPD Panel
Vosol	EPD Panel
VoSpire	EPD Panel
Votrient	EPD Panel
Zaroxolyn	EPD Panel
Varvara	EPD Panel
Viravan	EPD Panel
Naloxone	Primary Safety evaluator
Lorazepam	Primary Safety evaluator
Virazole	Primary Safety evaluator
Versacaps	Primary Safety evaluator
Renavaz	Primary Safety evaluator
Remoxy	Primary Safety evaluator
Loramyc	Primary Safety evaluator
Omontys	Primary Safety evaluator
Normaxan	Primary Safety evaluator
Levoxyl	Primary Safety evaluator
(b) (4)	Primary Safety evaluator
(b) (4)	Primary Safety evaluator

Our analysis of the 34 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for the names. We determined the 34 names will not pose a risk for confusion as described in Appendices D and E.

DMEPA communicated these findings to the Division of Biologic Oncology Products via e-mail on August 24, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Biologic Oncology Products on August 24, 2011, they stated no additional concerns with the proposed proprietary name, Voraxaze.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. However, 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.

The proposed proprietary name, Voraxaze, must be re-reviewed if BLA approval is delayed beyond 90 days.

If you have further questions or need clarifications, please contact Sue Kang, OSE project manager, at 301-796-4216.

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.

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. ***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. ***Access Medicine Database (http://www.accessmedicine.com/drugs.aspx)***

Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.

13. ***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.

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.

17. *LabelDataPlus Database (http://www.labeldataplus.com/index.php?ns=1)*

LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC (Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

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. [1]

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. [2] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the 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

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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.

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

monitoring the impact of the medication.[3] 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.

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

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

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.[4] 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.

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

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)].

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).

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.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name "Voraxaze"	When scripted may appear as:	When spoken may be interpreted as:
Capital 'V'	'U', 'L', 'N'	'F' sound
Lower case 'v'	'r', 'u'	'f' sound
Lower case 'o'	'a', 'c', 'e', 'u'	'Oh' sound, any vowel
Lower case 'r'	'v', 'u', 's', 'n', 'e'	'wr'
Lower case 'a'	'el', 'ci', 'cl', 'd', 'o', 'u'	Any vowel sound
Lower case 'x'	'a', 'd', 'f', 'k', 'n', 'p', 'r', 't', 'v', 'y'	'ks', 'kz', 's', 'z'
Lower case 'z'	'c', 'e', 'g', 'n', 'm', 'q', 'r', 's', 'v'	'c', 'x', 's' sound
Lower case 'e'	'a', 'i', 'l', 'p'	Any vowel sound

Appendix C: Prescription Study Results for Voraxaze conducted on 7/28/2011

Figure 1: Written and Verbal Samples

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Voraxaze (b) (4) intravenous bolus over 5 min	Voraxaze (b) (4) intravenous Bolus over 5 minutes
Outpatient Prescription: Voraxaze # 1 Vial Sig: (b) (4) IV bolus over 5 min	

Figure 2: FDA Prescription Study Written and Verbal Sample Results (22 Responses)

INPATIENT	VOICE	OUTPATIENT
Voraxarc	Berozase	Vorapaze
Voraxare	Varoxys	Voraxaye
Voraxare	Veroxase	Voraxaze
Voraxare	Veroxase	Voraxaze
Voraxare	Veroxes	Voraxaze
Voraxare	Veroxis	Voraxaze
Voraxare	Viroxase	Voraxaze
Vorazare		

Appendix D: Names eliminated from evaluation for the reasons listed (n=8)

	Proprietary Name	Similarity to Lixiana	Active Ingredient	Reason Eliminated
1	Renavaz	Look alike	Carvedilol and lisinopril)	(b) (4)
2	Normaxan	Look alike	Agomelatine	
3	Vorozole	Look alike	R83842	
4	Vasoxyl	Look alike	Methoxamine Hydrochloride	Product discontinued with no generic equivalents available.
5	Voreloxin	Look alike	Not available	Granted orphan drug status since 10/28/09 for treatment of acute myeloid leukemia. First in class quinolone derivative. No other information including product characteristics available on this product.

6	Versacaps	Look alike	Guaifenesin/Pseudoephedrine (300 mg/60 mg)	Product discontinued with no generic equivalents available.
7	Versaclear	Look alike	Not a drug product	A surgical laser instrument.
8	Loramyc	Look alike	Miconazole	(b) (4) [redacted]

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors (n=24).

PROPOSED NAME: Voraxaze (Glucarpidase) Powder for injection		STRENGTH: 1000 units/vial	USUAL DOSE: 50 units/kg, (b) (4) [redacted], by bolus intravenous injection over 5 minutes.
FAILURE MODE: **Name Confusion**		CAUSES: **(Potential reasons for name confusion that could lead to medication error)**	PREVENTION OF FAILURE MODE **(Reasons why the risk of medication error is minimized)**
1	Solaraze (Diclofenac Sodium) Gel, 3% Usual Dose Apply topically twice daily for 90 days.	Orthographic Both name consist of 8 letters, end with the letter string '-aze', and share the letter 'o' in the second position. Additionally, the letter string '-ax-' in Voraxaze may appear similar to the letter string '-ar-' in Solaraze when scripted. Also, when scripted in lower case, the letter 'V in Voraxaze may appear similar to the letter 'S' in Solaraze. Strength Single strength	Orthographic The upstroke 'l' in Solaraze may help differentiate the two names. Route of Administration Intravenous vs. topical Dosage Form Powder for injection vs. gel Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. twice daily Usual Dose 50 units/kg vs. one application

2	Naloxone (Established name for Narcan) Injection 0.4 mg/mL, 1 mg/mL Usual Dose Inject 0.1 mg to 2 mg intravenously, intramuscularly, or subcutaneously and titrated to response.	Orthographic Both names consist of eight letters. Additionally, the letter strings 'Vo-' and '-axaze' in Voraxaze may appear similar to the letter strings 'Na-' and '-oxone' in Naloxone when scripted. Overlap in Route of Administration Intravenous Dosage Form Injection Possible Overlap in Frequency of Administration One dose	Orthographic The upstroke 'l' in Naloxone may help differentiate the two names. Strength Single strength (1000 units/vial) vs. 0.4 mg/mL, 1 mg/mL Usual Dose 50 Units/kg vs. 0.1 mg to 2 mg
3	Lorazepam (Established name for Ativan) Tablets, oral solution, injection 0.5 mg, 1 mg, 2 mg, 0.5 mg/5 mL, 2 mg/mL, 4 mg/mL Usual Dose Anxiety, Insomnia: 2 mg to 6 mg per day in divided doses. Status epilepticus: 4 mg given slowly (2 mg/min) intravenously. Preanesthesia: 0.5 mg/kg up to a maximum of 4 mg IM at least 2 hours before procedure. For IV sedation, give 2 mg total or 0.044 mg/kg, whichever is less	Orthographic Both names share a downstroke in the 7th position ('z' in Voraxaze and 'p' in Lorazepam). Additionally, the letter string 'Voraxa-' in Voraxaze may appear similar to the letter string 'Loraze-' in Lorazepam when scripted. Overlap in Route of Administration Intravenous Overlap in Dosage Form Injection Possible Overlap in Frequency of Administration One dose Partial Numerical Overlap in the Usual Dose 50 units/kg (Voraxaze) vs. 0.5 mg/kg (Lorazepam) Partial Numerical Overlap in the Strength 50 units/kg vs. 0.5 mg	Orthographic The extra letter 'm' in Lroazepam makes the name Lorazepam appear longer than Voraxaze when scripted. Additionally, if letter Z in Lorazepam is scripted as a donwstroke, then the name Lorazepam will consist of 2 downstrokes vs. one downstroke in Voraxaze and that may help differentiate the two names.

4	Abraxane (Paclitaxel) Suspension for injection 100 mg/vial Usual Dose Inject 260 mg/m2 intravenously over 30 minutes every 3 weeks.	Orthographic Both names consist of eight letters. Additionally, the letter string '-axaze' in Voraxaze may appear similar to the letter string '-axane' in Abraxane when scripted. Partial Overlap in the Strength 1000 units/vial vs. 100 mg/vial Route of Administration Intravenous Dosage Form Injection	Orthographic The upstroke 'b' in Abraxane may help differentiate the two names. Frequency of Administration Bolus intravenous over 5 minutes x1 dose vs. over 30 minutes every 3 weeks. Usual Dose 50 units/kg vs. 260 mg/m2
5	Varivax (Varicella Virus Vaccine Live) Powder for injection 1350 PFU Usual Dose Inject one 0.5 mL subcutaneous injection followed by a second 0.5 mL injection 4 to 8 weeks later.	Orthographic All the letters in Varivax may appear similar to the letter string 'Voraxaz-' in Voraxaze when scripted. Strength Single strength Dosage Form Injection Possible Overlap in the Frequency of Administration One dose	Route of Administration Intravenous vs. subcutaneous Usual Dose 50 units/kg vs. 0.5 mL

6	Voriconazole (Established name for Vfend) Tablets, oral suspension, powder for injection 50 mg, 200 mg, 200 mg/5 mL, 200 mg/vial Usual Dose Oral: Load two doses of 400 mg 12 hours apart, followed by 200 mg every 12 hours. IV: Load two doses of 6mg/kg 12 hours apart, followed by 3 mg/kg every 12 hours.	Orthographic The name Voraxaze may appear similar to the letter string 'Voricona-' in Voriconazole when scripted. Overlap in Route of Administration Intravenous Overlap in the Dosage Form Injection Partial Numerical Overlap in the strength 50 units/kg vs. 50 mg	Orthographic The name Voriconazole appears longer than the name Voraxaze when scripted due to the extra letters 'o', 'l', and 'e' in Voriconazole. Additionally, the placement of the downstroke 'z' (7th position inVoraxaze and 9th position in Voriconazole) may help differentiate the two names. Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. two doses 12 hours apart Usual Dose 50 units/kg vs. 400 mg followed by 200 mg
7	Virazole (Ribavirin) Solution for inhalation 6 g/vial Usual Dose 20 mg/mL as the starting solution in the drug reservoir of SPAG-2 unit, with continuous aerosol administration for 12-18 hours per day for 3 to 7 days.	Orthographic Both names consist of eight letters. Additionally, the letter string 'Voraxa-' in Voraxaze may appear similar to the letter string 'Virazo' when scripted. Strength Single strength	Orthographic The upstroke 'l' in Virazole may help differentiate the two names. Route of Administration Intravenous vs. oral inhalation Dosage Form Injection vs. inhaler Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. 12 to 18 hours per day for 3 to 7 days Usual Dose 50 units/kg vs. 20 mg/mL

8	[redacted] (b) (4)		
9	Veramyst (Fluticasone Furoate) Nasal Spray 27.5 mcg Usual Dose Use 110 mcg (2 sprays per nostril) once daily (adults and adolescents 12 years and older), 55 mcg (1 spray per nostril) once daily (children 2 to 11 years)	Orthographic Both names consist of eight letters. The letter string 'Voraxa-' in Voraxaze may appear similar to the letter string 'Veram-' in Veramyst when scripted. Additionally, both names share a donwstroke in a similar position (z' in the 7th position in Voraxaze and 'y' in t he 6th position in Veramyst). Strength Single strength	Orthographic The upstroke't' in Veramyst may help differentiate the two names. Route of Administration Intravenous vs. intranasal Dosage Form Injection vs. nasal spray Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. once daily Usual Dose 50 units/kg vs. 100 mcg (2 sprays) or 55 mcg (1 spray).
10	Vesicare (Solifenacin Succinate) Tablets, 5 mg, 10 mg Usual Dose 5 to 10 mg orally once daily.	Orthographic Both names consist of eight letter and all the letters in Voraxaze may appear similar to all the letters in Vesicare when scripted. Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 5 mg	Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus Intravenous over 5 minutes x 1 dose vs. once daily

11	Veregen (Sinecatechins) Ointment, 15% Usual Dose Apply approximately a 0.5 cm strand 3 times daily to each wart.	Orthographic The letter string 'Vora-' in Voraxaze may appear similar to the letter string 'Vere-' in Veregen when scripted. Strength Single strength Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 0.5 cm	Orthographic The placement of the downstroke 'z' in Voraxaze (7th position) is different than the placement of the downstroke 'g' in Veregen (5th position) and may help differentiate the two names. Additionally, the cross stroke 'x' in Voraxaze may also help differentiate the two names. Route of Administration Intravenous vs. topical Dosage Form Injection vs. ointment Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. three times daily.
12	Noroxin (Norfloxacin) Tablets, 400 mg Usual Dose 400 mg orally every 12 hours 3 to 21 days (length of treatment depends on the type of infection being treated).	Orthographic The letter string 'Voraxaz-' in Voraxaze may appear similar to the name Noroxin when scripted. Strength Single strength	Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. every 12 hours Usual Dose 50 units/kg vs. 400 mg (or 1 tablet)
13	Vancenase (Beclomethasone Dipropionate) Inhalation solution 42 mcg (Discontinued, similar brands are available) Usual Dose One puff 2 to 4 times per day.	Orthographic The letter strings 'Vora-' and '-xaze' in Voraxaze may appear similar to the letter strings 'Vanc-' and '-nase' in Vancenase when scripted. Strength Single strength	Route of Administration Intravenous vs. oral inhalation Dosage Form Injection vs. inhaler Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. 2 to 4 times daily Usual Dose 50 units/kg vs. one puff

14	Norvasc (Amlodipine) Tablets 2.5 mg, 5 mg, 10 mg Usual Dose 2.5 mg to 10 mg orally once daily.	Orthographic The letter strings 'Vor-' and '-xaze' in Voraxaze may appear similar to the letter strings 'Nor-' and '-vasc' in Norvasc when scripted. Partial Numerical Overlap in the Strength 1000 units/vial vs. 10 mg Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 5 mg	Route of Administration Injection v s. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus intravenous over 5 minutes x 1 dose. Vs. once daily
15	Voltaren (Diclofenac Sodium) Ophthalmic solution, 0.1%, topical gel 1%, tablets, 25 mg, 50 mg, 75 mg Usual Dose Oral: Usually 25 mg PO four times daily with an additional 25 mg dose at bedtime, if needed. Gel: 4 g for each knee, ankle, or foot four times daily. Apply 2 g for each elbow, wrist, or hand four times daily. Drops: 1 drop to the affected eye(s) four times daily for 2 weeks	Orthographic Both names consist of eight letter and share the letter string 'Vo-'. Additionally, the letter string '-aze' in Voraxaze may appear similar to the letter string '-are-' in Voltaren when scripted. Also the position of the cross stroke 'x' in Voraxaze (5th position) is similar to the position of the cross stroke 't' in Voltaren (4th position). Possible Overlap in Strength Single strength (if Voltaren gel or ophthalmic solution) Possible Overlap in the Usual Dose 50 units/kg vs. 50 mg (Voltaren tablets)	Orthographic The upstroke 'l' in Voltaren may help differentiate the two names. Route of Administration Intravenous vs. oral, topical, or ocular Dosage Form Injection vs. tablets, gel, or drops Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. four times daily.

16	Voluven (Hetastarch in Sodium Chloride) Solution for injection 6%/9% Usual Dose Initially, 30-60 g (500-1000 ml) IV infusion. Do not exceed 1.2 g/kg (20 ml/kg) or 90 g (1500 ml) per day. A rate up to 1.2 g/kg/hour (20 ml/kg/hour) may be used in acute hemorrhagic shock. A slower rate is used in septic shock or burns.	Orthographic Both names share the letter string 'Vo-'. Additionally, the letter string '-axaz-' in Voraxaze may appear similar to the letter string '-uven' in Voluven when scripted. Strength Single strength Route of Administration Intravenous Dosage Form Injection Possible Overlap in the Frequency of Administration One dose	Orthographic The upstroke 'l' in Voluven may help differentiate the two names Usual Dose 50 units/kg vs. 30 to 60 gram or 1.2 g/kg/hour
17	Vosol (Hydrocortisone Acetic Acid) Otic drops 1%/2% Usual Dose 3-5 drops into the affected ear every 4-6 hours.	Orthographic The letter string 'Vora-' in Voraxaze may appear similar to the letter string 'Voso-' in Vosol when scripted. Strength Single strength Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 5	Orthographic The name Voraxaze appears longer than the name Vosol when scripted due to the extra letters 'x', 'a', and 'z' in Voraxaze. Route of Administration Intravenous vs. otic Dosage Form Injection vs. drops Frequency of Administration Bolus intravenous over 5 minutes vs. every 4 to 6 hours.

18	Votrient (Pazopanib) Tablets 200 mg Usual Dose 400 mg by mouth once daily.	Orthographic Both names consist of eight letters and share the letter string 'Vo-'. Additionally, the letter string '-ra-' in Voraxaze may appear similar to the letter string '-ri-' in Votrient when scripted. Strength Single strength	Orthographic 3 upstrokes ('V', 't', 't') and not downstrokes in Votrient vs. one upstroke ('V') and one downstroke ('z') in Voraxaze. Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. once daily. Usual Dose 50 units/kg vs. 400 mg (or 1 tablet)
19	VoSpire (Albuterol Sulfate) Tablets 4 mg, 8 mg Usual Dose 4 to 8 mg orally every 6 to 8 hours (maximum 32 mg/day)	Orthographic Both names share the letter string 'Vo-'. Additionally, the letter string '-axaze' in Voraxaze may appear similar to the letter string '-spire' in Vospire when scripted.	Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Strength 1000 units/vial vs. 4 mg and 8 mg Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. every 6 to 8 hours Usual Dose 50 units/kg vs. 4 to 8 mg (or 1 to 2 tablets)

20	Zaroxolyn (Metalazone) Tablets 2.5 mg, 5 mg, 10 mg Usual Dose Initially, 5-10 mg PO once daily. If a loop diuretic is used concomitantly, the initial dose is 2.5 mg PO once daily. If needed, titrate dosage up to 20 mg/day.	Orthographic The letter string 'Voraxa-' in Voraxaze may appear similar to the letter string 'Zaroxo-' in Zaroxolyn when scripted. Additionally, both names share a donwstroke in a similar position ('z' in the 7th position in Voraxaze and 'y' in the 8th position in Zaroxolyn). Partial Numerical Overlap in the Strength 1000 units/vial vs. 10 mg Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 5 mg	Orthographic The upstroke 'l' in Zaroxolyn may help differentiate the two names. Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. once daily.
21	Varvara (Common garden basil. Name found in the Natural Medicines database. Used for stomach spasms, head colds, kidney conditions, to promote blood circulation, and to treat snake and insect bite.) Usual Dose 1 cup of the fresh brewed tea 2 to 3 times a day between meals. The tea is prepared by steeping 2 to 4 grams in 150 mL boiling water for 10 to 15 minutes. and straining.	Orthographic The letter strings 'Vor-' and '-xaze' in Voraxaze may appear similar to the letter strings 'Var-' and '-vara' in Varvara when scripted. Strength Single strength	Route of Administration Intravenous vs. oral Dosage Form Injection vs. leaves Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. 2 to 3 times daily. Usual Dose 50 units/kg vs. 1 cup

22	Viravan PDM (Dextromethorphan Hydrobromide, Pseudoephedrine Hydrochloride, Pyrilamine Maleate) Oral suspension 15 mg-30 mg-20 mg/ 5 mL Usual Dose One teaspoonful orally every 12 hours.	Orthographic The letter string 'Voraxaz-' in Voraxaze may appear similar to the name Viravan (if the modifier PDM is omitted). Strength Single strength	Orthographic If included, the modifier 'PDM' may help differentiate the two names. Route of Administration Intravenous vs. oral Dosage Form Injection vs. oral suspension Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. every 12 hours. Usual Dose 50 units/kg vs. one teaspoonful
23	Levoxyl (Levothyroxine) Tablets 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg,175 mcg, 200 mcg, and 300 mcg Usual Dose 25 mcg to 300 mcg orally once daily.	Orthographic The letter string 'Vorax-' in voraxaze may appear similar to the letter string 'Levox-' in Levoxyl when scripted. Additionally, the letter string '-ze' in Voraxaze may appear similar to the letter string '-yl' when scripted. Partial Numerical Overlap in Strength 1000 units/vial vs. 100 mcg Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 50 mcg	Route of Administration Intravenous vs. oral Dosage Form Injection vs. tablets Frequency of Administration Bolus intravenous over 5 minutes x 1 dose vs. once daily

24	Vancocin (Vancomycin) Powder for injection, pulvule, solution for injection, powder for oral solution Powder for injection: 10 gram, 1 gram, 500 mg, Pulvule: 125 mg, 250 mg, Solution for injection: 1 g/200 mL, 500 mg/100 mL Usual Dose Adults and Adolescents: 125-500 mg PO every 6 hours for 7-10 days. Infants and children: 40 mg/kg/day PO in divided doses every 6 hours for 7-14 days. IV dose: Adults and Children weighing greater than 27 kg: 10-15 mg/kg. Usual dose in average size adults is 500-1000 mg. Children weighing less than 27 kg: 20 mg/kg	Orthographic Both names consist of eight letters. The letter strings 'Vora-' and '-xaz-' in Voraxaze may appear similar to the letter strings 'Vanc-' and '-cin' in Vancocin when scripted. Partial Numerical Overlap in Strength 1000 units/vial vs. 10 gram Partial Numerical Overlap in the Usual Dose 50 units/kg vs. 500 mg Overlap in the Route of Administration Intravenous Overlap in the Dosage Form Injection	Frequency of Administration Bolus Intravenous over 5 minutes x 1 dose vs. 7 to 10 days.

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*** This is proprietary and confidential information that should not be released to public

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(b) (4)

[redacted]

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