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APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date: June 18, 2013

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Drug Name and Strength(s): Varithena (Polidocanol Injectable Microfoam) 1%

Application Type/Number: NDA 205098

Applicant/Sponsor: BTG International Inc.

OSE RCM #: 2013-746

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Varithena, 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

On December 16, 2012, the Applicant submitted a request for proprietary name review under IND 063420 for the name Varisolve. However, during the initial steps of the proprietary name review process, the Office of Prescription Drug Promotion (OPDP) did not recommend the use of the proposed proprietary name Varisolve because it overstates the efficacy of the drug product. The unacceptability of the proposed proprietary name, Varisolve, was communicated to the Sponsor on February 21, 2012.

On August 17, 2012, the Applicant submitted a new request for proprietary name review under IND 063420 for the name, Varithena, which was found to be acceptable under OSE RCM 2012-2058 dated February 13, 2013.

On February 4, 2013, the Applicant submitted NDA 205098, and then on March 21, 2013, they submitted a request for proprietary name review for Varithena which is the subject of this review. Since our previous review, the product characteristics have changed [REDACTED] (b) (4). Under the NDA, the Applicant proposes [REDACTED] (b) (4) 1%.

1.2 PRODUCT INFORMATION

The following product information is provided in the March 21, 2013 proprietary name submission.

- Active Ingredient: Polidocanol
- Indication of Use: Treatment of varicose veins and visible varicosities
- Route of Administration: For intravenous use only. Varithena is intended for intravenous injection using ultrasound guidance, administered via a single cannula into the lumen of the target incompetent trunk veins or by direct injection into varicosities.
- Dosage Form: Injectable Microfoam (proposed)
- Strength: 1 %
- Dose and Frequency: The maximum recommended microfoam volume per treatment session is 15 mL, divided into aliquots of up to 5 mL. Single treatment session and potential subsequent follow up treatment sessions should be separated by a minimum of 5 days.
- How Supplied: Varithena is supplied in a convenience box that contains:
 - A Tyvek pouch containing two sterile, connected 303 mL aluminum alloy canisters: one containing [REDACTED] (b) (4) Polidocanol Solution under a carbon dioxide atmosphere, the second containing pressurized Oxygen at approximately

5.4 bar absolute. The Connector joins the two canisters and activates the product.

A canister of Varithena generates 90 mL of microfoam which, following purging instructions contained in the Instructions For Use (IFU) is sufficient to yield 45 mL of usable microfoam for injection.

- Three Microfoam Transfer Units to dispense microfoam;
- Three administration boxes each containing:
 - Three 10 mL silicone-free Luer syringes;
 - A 20-inch Manometer Tube;
 - Two Compression Pads.
- Storage: Room temperature 15 °C to 25 °C
- Container and Closure Systems: The product is a bi-canister unit format consisting of the following components:
 - A “Polidocanol Canister” containing a 1% (b) (4) polidocanol solution held under an atmosphere (approximately 1.2 bar absolute) of carbon dioxide.
 - An “Oxygen Canister” containing oxygen at approximately 5.4 bar absolute which is used to pressurize the polidocanol canister immediately prior to use so as to permit generation of the microfoam.
 - A connector (b) (4) provides a mechanism for oxygen gas transfer from the “Oxygen Canister” to the “Polidocanol Canister”.

2. RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Division of Cardiovascular and Renal Products (DCRP) concurred with the findings of OPDP’s promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 *United States Adopted Names (USAN) SEARCH*

The April 22, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Varithena, is derived from “varicose veins”. Since the proposed product is indicated for the treatment of varicose veins, the derivation of the name is consistent with the indication. Therefore, OPDP and DMEPA do not find the name misleading.

2.2.3 FDA Name Simulation Studies

A total of 75 practitioners participated in FDA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. In the Written study group, 23 out of 56 of the participants correctly identified the name as ‘Varithena’. The most common misinterpretation included mistaking the uppercase letter ‘V’ for the uppercase vowel ‘O’. Only 1 out of the 19 participants in the Verbal study group correctly identified the name as ‘Varithena’. The misinterpretations in the voice study included the vowels ‘a, i, and e’ being mistaken for each other. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, May 14, 2013 e-mail, the Division of Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

The proposed product characteristics for Varithena have changed since our previous review of the name. (b) (4)

The Applicant (b) (4) proposes a single strength, 1%, for Varithena. Therefore, we evaluated the previously identified names (see OSE Review 2012-2058 dated February 13, 2013) and determined the change in product characteristic does not alter our previous conclusion regarding the acceptability of the proposed proprietary name.

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Varithena. Table 1 lists the newly identified names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Varithena, identified by the primary reviewer, the Expert Panel Discussion (EPD), FDA Prescription Simulation, and other review disciplines.

Table 1: Collective List of Potentially Similar Names from Primary Reviewer, Expert Panel Discussion (EPD), FDA Prescription Simulation, and Other Disciplines not previously evaluated in OSE Review #2012-2058

<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Look Similar (n=12)					
(b) (4)	FDA	Zarontin	FDA	Vasculera	FDA
Lanthanum	FDA	Zetonna	FDA	Varenicline	FDA
Verdeso	FDA	Vinorelbine	FDA	Veratrine	FDA
Varicella	FDA	Verilizer	FDA	Venitone	FDA
Look and Sound Similar (n=2)					
Varitonin	FDA	Verithin	FDA		

Our analysis of the 14 new names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined none of the 14 names pose a risk for confusion as described in Appendices D through E.

2.2.6 Communication of DMEPA’s Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on May 17, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Cardiovascular and Renal Products (DCRP) on May 20, 2013, they stated no additional concerns with the proposed proprietary name, Varithena.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Cheryle Milburn, OSE Project Manager, at 301-796-2084.

3.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your March 21, 2013, submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

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

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

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

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

5. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

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

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and “Chemical Type 6” approvals.

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.²

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

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

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

Type of Similarity	Considerations when Searching the Databases		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

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

1. Database and Information Sources

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

2. Expert Panel Discussion

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

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

3. FDA Prescription Simulation Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

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

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

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

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

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

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name may be confusing, misleading, cause or contribute to medication errors.

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

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

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

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

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

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Varithena	Scripted May Appear as	Spoken May Be Interpreted as
Uppercase V	U, N, L, M, R, W, X, S, Z, O	F
Lower case v	r, u, w, n	f
a	el, ci, cl, d, o, u, c, e, er, ce, x, s	Any vowel
r	s, n, e, ,v, x, t, w, i, c	rer
i	l, e, o, u, a, c, r	eye, y
t	r, f, x, A, k, l	tee, tea
h	k, b, n, L	hah
e	a, i, l, o, u, l, c, p	Any vowel
n	m, u, x, r, h, s, v, w	dn, gn, kn, mn, pn
Letter strings		
ar	en, or, cu, w	agh, r, or
ri	u, w, v, n	ree, re, rew
en	ar, in, ea, ox m, w	and, an, on
na	m, non, rm, sen	---
th	---	f
thena	ulena, them, thenon, therm, thesen	zina, zena, sina, sena, fina, fena, pena, pina, tina, tena, cena, cina, dina, dena

Appendix C: Prescription Simulation Samples and Results

Figure 1. Varithena Study (Conducted on 5/3/13)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Inpatient Medication Order:</u></p> <p><i>Varithena 1st Inject 5ml into great saphenous veins under ultrasound once</i></p>	<p>Varithena Bring to Clinic Dispense #1</p>
<p><u>Outpatient Prescription:</u></p> <div data-bbox="196 743 922 1199" style="border: 1px solid black; padding: 5px;"> <p>Patient _____ Date _____ Address _____</p> <p>R_x</p> <p><i>Varithena #1</i> <i>Bring to clinic</i></p> <p>Dr. <i>ose</i> _____ Address _____ Telephone _____</p> <p>Refill(s): _____ DEA No. _____</p>  </div>	

Study Name: Varithena

190 People Received Study

75 People Responded

	Total	30	19	26	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL	
OARITHENA	15	0	0	15	
OARITHNA	1	0	0	1	
RANITHENA	0	0	1	1	
VANITHENA	0	0	2	2	
VANITHENA 1%	0	0	1	1	
VANITHERA	0	0	1	1	
VANTHENA	0	0	1	1	
VARATHENA	0	1	0	1	
VARITHEM	0	0	3	3	
VARITHEMA	0	0	1	1	
VARITHENA	14	1	9	24	
VARITHENO	0	0	2	2	
VARITHENON	0	0	1	1	
VARITHERM	0	0	1	1	
VARITHERM 1%	0	0	1	1	
VARITHESEN	0	0	1	1	
VERAFINA	0	1	0	1	
VERATHENA	0	12	0	12	
VERATHINA	0	1	0	1	
VERETHINA 1 VIAL	0	1	0	1	
VERITHENA	0	2	0	2	
VERITHENA 1%	0	0	1	1	

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

No.	Proprietary Name	Active Ingredient	Similarity to Varithena	Failure Preventions
1.	(b) (4)			
2.	Zarontin	Ethosuximide	Orthographic	The name pair has sufficient orthographic differences.
3.	Zetonna	Ciclesonide	Orthographic	The name pair has sufficient orthographic differences.
4.	Varicella	Marketed as Varicella Virus Vaccine Live or Varicella-Zoster Immune Globulin (Human)	Orthographic	The name pair has sufficient orthographic differences.
5.	Varenicline	generic name of Chantix®	Orthographic	The name pair has sufficient orthographic differences.
6.	Veratrine	Veratrum Alkaloid plant	Orthographic	Name identified in Micromedex Poisindex database. Unable to find product characteristics in commonly used drug databases.
7.	Verilizer	Trademark by Novartis IC 005. US 006 018 044 046 051 052. G & S: Pharmaceutical preparations for the treatment of disorders of the respiratory system or IC 010. US 026 039 044. G & S: Medical apparatus for diagnosing or treating respiratory conditions; Medical apparatus for facilitating the inhalation of pharmaceutical preparations.	Orthographic	Name identified in USPTO database. Unable to find product characteristics in commonly used drug databases.
8.	Venitone	Trademark by Western Holdings IC 005. US 006	Orthographic	Name identified in USPTO database. Unable to find

		018 044 046 051 052. G & S: Dietary supplements		product characteristics in commonly used drug databases.
9.	Verithin	Trademark By National Vision IC 009. US 021 023 026 036 038. G & S: Eyeglass Lenses; Optical Lenses. First Use: 19980101. First Use In Commerce: 19980101	Orthographic	Name identified in USPTO database. Name is not designated for a drug product. Unable to confirm as a drug name in any commonly used drug databases.

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

No.	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatments sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
1.	<p>Varitonin (Vitamin C, Horse Chestnut Seed, Hesperidin Methyl Chalcone, Gotu Kola Leaf, Butcher’s Broom Rhizome) Capsules</p> <p>Strength(s): Vitamin C (250 mg), Horse Chestnut Seed (250 mg), Hesperidin Methyl Chalcone (125 mg), Gotu Kola Leaf (60 mg), Butcher’s Broom Rhizome (50 mg)</p> <p>Usual Dose: 1 to 2 capsules daily or as directed by physician</p>	<p>Orthographics: Both names have identical beginning letter strings ‘Varit’ and similar in length.</p> <p>Phonetics: Both names have 4 syllables and identical first two syllables from the same letter string ‘Va-ri’.</p> <p>Strength: Both drugs are single strength products so the strength may be omitted on a prescription</p> <p>Dose: Numerical overlap between dose of ‘1’ cap for Varitonin and ‘10 mL’ for Varithena</p> <p>Route of administration: Both drugs are single route</p>	<p>Orthographics: Varitonin lacks the second upstroke letter ‘h’ found in Varithena creating a different suffix (‘onin’ vs. ‘hena’) which differentiates it from each other.</p> <p>Phonetics: Both names have different last two syllables due to different sounds from the letter string ‘ton’ vs. ‘then’ and from ‘in’ vs. ‘ah’.</p> <p>Frequency of administration: One to three injections in one treatment session and may repeat in 5 days vs. once daily</p> <p>Setting of use: Varithena can only be administered intravenously by a trained and certified physician</p>

No .	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatments sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
		<p>products so the route of administration may be omitted on a prescription</p>	<p>under ultrasound guidance and subjected to a REMS program vs. Varitonin that can be obtained and administered orally by the patient</p>
2.	<p>Vinorelbine (Vinorelbine) Injection Solution</p> <p>Strength(s): 10 mg/mL</p> <p>Usual Dose: 30 mg/m² administered weekly by intravenous injection over 6 to 10 minutes as a single agent, or 25 mg/m² in combination with cisplatin given every 4 weeks or 30 mg/m² in combination with cisplatin given on days 1 and 29 then every 6 weeks</p>	<p>Orthographics: Both names have orthographically similar beginning letter strings ‘Vari’ vs. ‘Vin’, ending letter strings ‘ena’ vs. ‘ine’ when scripted, and contain two adjacent upstroke letters (‘th’ vs. ‘lb’) in their infixes.</p> <p>Strength: Both drugs are single strength products so the strength may be omitted on a prescription and there is numerical similarity between ‘10’ mg/mL and ‘1’% (although the units may differentiate)</p> <p>Route of administration: Both drugs are administered intravenously</p>	<p>Orthographics: Vinorelbine has 6 letters preceding the double upstroke letter string vs. only 4 letters in the Varithena name. This length difference in the two infixes helps to differentiate it from each other.</p> <p>Dose: No overlap since Vinorelbine dose must be calculated at either 25 mg/m² or 30 mg/m² while Varithena dose is 5 mL, 10 mL, or 15 mL.</p> <p>Frequency of administration: One to three injections in one treatment session and may repeat in 5 days vs. weekly, or every 4 weeks, or on days 1 and 29 then every 6 weeks.</p>

No .	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatments sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
			<p>Setting of use: Varithena can only be administered intravenously by a trained and certified physician under ultrasound guidance and subjected to a REMS program vs. Vinorelbine is an oncology drug that must be administered alone or with cisplatin at pre-determined dosing intervals</p>
3.	<p>Lanthanum Carbonate (generic name of Fosrenol®) Chewable Tablets</p> <p>Strength(s): 500 mg, 750 mg, and 1000 mg</p> <p>Dose and Frequency: Initial total daily dose of Fosrenol is 1500 mg to 3000 mg (max doses up to 4500 mg) to be titrated in increments of 750 mg/day taken as divided doses with or immediately after food</p>	<p>Orthographics: Both names have orthographically similar beginning letter strings ‘Vari’ vs. ‘Lan’, and contain identical upstroke pair ‘th’ in their infixes.</p> <p>Strength: Numerical overlap between ‘1000’ mg and ‘1’% since ‘00’ may appear as ‘%’ in scripted handwriting</p> <p>Dose: Numerical similarity between dose of ‘1’ tab or ‘1000’ mg’</p>	<p>Orthographics: Lanthanum has an extra letter ‘m’ at the end of its name not found in Varithena which lengthens the suffix.</p> <p>Frequency of administration: One to three injections in one treatment session and may repeat in 5 days vs. divided doses with or immediately after food every day</p> <p>Setting of use: Varithena can only be administered intravenously by a</p>

No .	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatments sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
		<p>for Lanthanum vs. '10 mL' for Varithena or '500 mg' for Lanthanum vs. '5 mL' for Varithena</p> <p>Route of administration: Both drugs are single route products so the route of administration may be omitted on a prescription</p>	<p>trained and certified physician under ultrasound guidance and subjected to a REMS program vs. Lanthanum that can be obtained and administered orally by the patient</p>
4.	<p>Verdeso (Desonide) Foam</p> <p>Strength(s): 0.05%</p> <p>Dose and Frequency: A thin layer of Verdeso Foam should be applied to the affected area(s) twice daily. Shake the can before use. Verdeso Foam should be dispensed by inverting the can (upright actuation will cause loss of the propellant which may affect product delivery). Dispense the smallest amount of foam necessary to adequately cover the affected</p>	<p>Orthographics: Both names have orthographically similar beginning letter string 'Var' vs. 'Ver' when scripted, contain an upstroke letter 'd' vs. 't' in the middle of the names, and end with orthographically similar letter string 'ena' vs. 'eso'.</p> <p>Strength: Both drugs are single strength products so the strength may be omitted on a prescription</p> <p>Route of administration:</p>	<p>Orthographics: Verdeso is missing the second upstroke letter 'h' which creates a different shape to the infix compared to Varithena.</p> <p>Frequency of administration: One to three injections in one treatment session and may repeat in 5 days vs. twice daily.</p> <p>Dose: No overlap in dose (smallest amount of foam vs. 5 mL, 10 mL, or 15 mL)</p> <p>Setting of use: Varithena can only be</p>

No .	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatments sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
	<p>area(s) with a thin layer</p>	<p>Both drugs have only one route of administration that may be omitted from a prescription.</p> <p>Dosage formulation: Both products are foam formulation.</p>	<p>administered intravenously by a trained and certified physician under ultrasound guidance and subjected to a REMS program vs. Verdeso that can be obtained and administered topically by the patient</p>
5.	<p>Vasculera (Diosmiplex) Tablets</p> <p>Strength(s): 630 mg</p> <p>Dose and Frequency: <i>For dietary management of Chronic Venous Insufficiency (CVI): 1 tablet per day</i> <i>For symptomatic flares of CVI: 1 tablet 3 times daily for 4 days followed by 1 tablet twice daily for 9 days</i> <i>For chronic management of hemorrhoidal disease: 1 tablet daily</i></p> <p>This product is a medical food.</p>	<p>Orthographics: Both names have orthographically similar beginning letter strings ‘Var’ vs. ‘Vas’, ending letter strings ‘ena’ vs. ‘era’, and contain an upstroke letter ‘l’ in their infixes.</p> <p>Strength: Both drugs are single strength products so the strength may be omitted on a prescription</p> <p>Dose: Numerical similarity between dose of ‘1’ tab for Vasculera vs. ‘10’ mL for Varithena</p> <p>Route of administration: Both drugs are single route</p>	<p>Orthographics: Vasculera lacks the second upstroke letter and has an extra letter preceding the upstroke letter ‘l’ which change the shape of the infix (‘cul’ vs. ‘ith’) and differentiate it from Varithena</p> <p>Frequency of administration: One to three injections in one treatment session and may repeat in 5 days vs. once daily or three times daily</p> <p>Setting of use: Varithena can only be administered intravenously by a trained and certified physician under ultrasound guidance and subjected to a REMS program</p>

No .	<p>Proposed name: Varithena (Polidocanol)</p> <p>Dosage Form: Injectable Microfoam</p> <p>Strength: 1%</p> <p>Usual Dose: For intravenous use only. The maximum recommended volume per treatment session is 15 mL. Individual injections of Varithena should not exceed 5 mL. Further treatments may be necessary if the extent of the varicose veins requires more than 15 mL of Varithena. Treatment sessions should be separated by a minimum of 5 days.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name Confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
		<p>products so the route of administration may be omitted on a prescription</p>	<p>vs. Vasculera that can be obtained and administered orally by the patient</p>

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/s/

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