

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205109Orig1s000

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--Final

Date: September 16, 2013

Reviewer: Kimberly DeFronzo, RPh, MS, MBA
Division of Medication Error Prevention and Analysis

Team Leader: Irene Z. Chan, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Drug Name(s) and Strength(s): Velphoro (b) (4) Chewable Tablet
500 mg

Application Type/Number: NDA 205109

Applicant: Vifor Pharma

OSE RCM #: 2013-1570

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

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Velphoro, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Velphoro, acceptable in OSE Review RCM #2013-305 dated June 6, 2013.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review RCM #2013-305. We note that none of the proposed product characteristics were altered. However, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. The searches of the databases yielded no new names thought to look similar to Velphoro and represent a potential source of drug name confusion.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any USAN stems in the proposed proprietary name, as of September 5, 2013.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Velphoro, did not identify any vulnerability that would result in medication errors. Thus, DMEPA has no objection to the proprietary name, Velphoro, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Cardiovascular Renal Products (DCRP) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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

4 REFERENCES

1. ***OSE Review RCM #2013-305 dated June 6, 2013, Kimberly DeFronzo, RPh, MS, MBA***
2. ***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.
3. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?>)
USAN Stems List contains all the recognized USAN stems.
4. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***
Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

/s/

KIMBERLY A DE FRONZO
09/16/2013

IRENE Z CHAN
09/16/2013

**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 6, 2013

Reviewer: Kimberly DeFronzo, RPh, MS, MBA
Division of Medication Error Prevention and Analysis

Team Leader: Irene Z. Chan, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Director: Carol Holquist, RPh
Division of Medication Error Prevention and Analysis

Drug Name and Strength (s): Velphoro (PA21) Chewable Tablet
500 mg

Application Type/Number: NDA 205109

Sponsor: Vifor Pharma

OSE RCM #: 2013-305

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Velphoro, 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 May 25, 2012, Vifor submitted a request for Proprietary Name Review for this product under IND 075610 for the primary name, (b) (4), and the alternate name, Velphoro. The name (b) (4) was found to be unacceptable by DMEPA due to

(b) (4)

On March 13, 2013, Vifor submitted a new proprietary name request for the alternate name, Velphoro, under NDA 205109. The dosing submitted for the Velphoro proprietary name request (1500 mg/day taken as 500 mg three times daily with meals) was a change from the dosing submitted under the IND for the (b) (4) name request (b) (4)

(b) (4)

1.2 PRODUCT INFORMATION

The following product information is provided in the March 13, 2013 proprietary name submission.

- Active Ingredient: PA21 (preferred proposed USAN name: (b) (4))
- Indication of Use: Control of serum phosphorus levels in patients with end-stage renal disease (ESRD)
- Route of Administration: Oral
- Dosage Form: Chewable Tablet
- Strength: 500 mg
- Dose and Frequency: The recommended starting dose is 1500 mg (3 tablets) per day, administered as 1 tablet (500 mg) 3 times daily with meals. Serum phosphorus levels should be monitored and the dose titrated in decrements or increments of 500 mg (1 tablet) per day as needed until acceptable serum phosphorus level (less or equal to 5.5 mg/dL) is reached, with regular monitoring afterwards. Titration can be started as early as 1 week after treatment initiation. Based on clinical studies, on average patients required 3 to 4 tablets (1,500 mg to 2,000 mg) a day to control serum phosphorus levels. The highest daily dose studied in a Phase 3 clinical trial in ESRD patients was 6 tablets (3,000 mg) per day.

- How Supplied: Brown, circular, bi-planar, chewable tablets embossed with “PA 500” on one side. Each tablet contains 500 mg iron as (b) (4) and will be packaged in bottles of 30 tablets or 90 tablets and in blister cartons of 30 tablets or 90 tablets (6 tablets per blister card).
- Storage: Store at 25°C (77°F) with excursions permitted to 15°C to 30°C (59°F to 86°F). Store in the original package and keep the bottle tightly closed in order to protect from moisture. The shelf life is 18 months. Do not use after expiration date on the package.
- Container and Closure Systems: There are 2 container closure systems for the drug product. The bottle configuration consists of a high density polypropylene bottles (HDPE) bottle (b) (4). The blister configuration consists of (b) (4). The bottles or blister units are contained inside a paperboard carton.

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 Cardiovascular 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 May 14, 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 *Established Name*

There is no established name for this product yet. The current proposed USAN names include (b) (4) Sucroferric Oxyhydroxide, (b) (4) and Sucroferric Oxyhydroxide, with the preferred name of (b) (4)

2.2.3 *Components of the Proposed Proprietary Name*

The Applicant indicated in their submission that the proposed name, Velphoro, is not derived from any concept. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.4 FDA Name Simulation Studies

A total of 93 practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products. The interpretations also did not appear or sound similar to any currently marketed products or products in development. In the Outpatient (written) study group, 9 out of 34 participants correctly identified the name as 'Velphoro'. Nearly all of the participants (30 out of 31) in the Inpatient (written) study group correctly identified the name as 'Velphoro'. However, no one out of the 28 participants in the Voice (verbal) study group correctly identified the name as 'Velphoro'.

The misinterpretations in the written studies included the lowercase vowel 'o' being mistaken for the other vowels 'u, e', and the lowercase letter string 'ro' being mistaken for the lowercase letter 'n' or 'w'.

The misinterpretations in the voice study included the pronunciation from the letter string 'Vel' being mistaken for 'Val', 'Nel', 'Nal', 'Mel', 'Zal', or 'Zel', and 'ph' being mistaken for 'f'. These interpretations were considered in our search strategies for similar names and assessment of similar names (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, February 12, 2013 e-mail, the Division of Cardiovascular Renal Products (DCRP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.6 Failure Mode and Effects Analysis (FMEA) of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Velphoro.

Table 1 lists the names identified to have potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Velphoro, by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from an external study conducted by Drug Safety Institute, Inc. (DSI) that were not identified by DMEPA, but considered names of concern requiring further evaluation.

| Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study) | | | | | |
|---|------------------|-------------|---------------|---------------------------|------------------|
| <i>Name</i> | <i>Source</i> | <i>Name</i> | <i>Source</i> | <i>Name</i> | <i>Source</i> |
| Look Similar to Velphoro (n=18) | | | | | |
| Tylenol | FDA | Zelboraf | FDA | Vol-Plus | FDA |
| Vilofane-DP 7.5 | FDA | Veltane | FDA | Zelapar | FDA |
| Valproic Acid | FDA | Votrient | FDA | (b) (4) | FDA |
| (b) (4) | EPD | Voltaren | FDA | Valerian | FDA |
| Naldecon | FDA | Valtrex | FDA | Veletri | FDA |
| Valtropin | FDA, External | Edurant | External | Valturna | External |
| Sound Similar to Velphoro (n=4) | | | | | |
| Venlafaxine | External | Valproate | External | Aquaphor | External |
| Valchlor | FDA | | | | |
| Look and Sound Similar to Velphoro (n=6) | | | | | |
| Velphoro | FDA | Relpax | External | Velcade | FDA, External |
| Venofer | External | Vitapro | External | Zohydro ER ^{***} | FDA |

Based on the FMEA of the 28 names contained in Table 1, DMEPA determined none of the 28 names will pose a risk for confusion as described in Appendices D and E.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products via e-mail on April 18, 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 on April 25, 2013, they stated no additional concerns with the proposed proprietary name, Velphoro.

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

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 Cherye Milburn, OSE project manager, at 301-796-2084.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Velphoro, 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 13, 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/about/MedErrors.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, Velphoro | Scripted May Appear as | Spoken May Be Interpreted as |
|---------------------------|---|----------------------------------|
| V | X, Z, J, L, M, U, Y, N, W, E, R, B | B, F, C, Ph, L, T, D, N, M, Z, W |
| v | x, h, la, r, u, w, n, m, s, z, c, b, y, j | b, f, c, ph, l, t, d |
| e | a, c, i, l, o, p, u | Any vowel |
| l | b, e, s, a, P, i, d, t, p, i, I, c | r |
| p | y, g, j, l, q, x, z, yn, ys | D, b, t, v, n |
| h | b, k, n, L | ha, huh |
| o | a, e, u, c | Oh, any vowel |
| r | n, s, v, x, z, i, c, e | l |
| Letter String | | |
| el | d, b, a, u | L |
| p | jo, ja, yn, ys | D, b, t, v, n |
| ph | | f |
| or | | awe |
| phoro | phon, phore, phow, phro | foral, farol, foro, poro, fouro |
| ro | n, w | row |

Appendix C: Prescription Simulation Samples and Results

Figure 1. Velphoro Study (Conducted on 2/8/13)

| Handwritten Requisition Medication Order | Verbal Prescription |
|---|--|
| <p><u>Inpatient Medication Order:</u> <i>Velphoro 1000mg po three times daily w/ meals</i></p> | <p>Velphoro 500 mg Chew 1 tablet tid with meals Dispense #90</p> |
| <p><u>Outpatient Prescription:</u></p> <div style="border: 1px solid black; padding: 5px;"> <p>Patient _____ Date _____ Address _____</p> <p>R</p> <p><i>Velphoro</i> <i>500 mg chew + tab tid</i> <i>with meals</i> <i>#90</i></p> <p>Refill(s): _____ Dr. _____ DEA No. _____ Address _____ Telephone _____</p> </div> | |

Study Name: Velphoro

193 People Received Study

93 People Responded

Study Name: Velphoro

| | Total | 31 | 28 | 34 | |
|-----------------------|------------------|--------------|-------------------|--------------|--|
| INTERPRETATION | INPATIENT | VOICE | OUTPATIENT | TOTAL | |
| MELFORAL | 0 | 1 | 0 | 1 | |
| NALFAROL | 0 | 1 | 0 | 1 | |
| NALFORO | 0 | 1 | 0 | 1 | |
| NELFORO | 0 | 1 | 0 | 1 | |
| NELSPORO | 0 | 1 | 0 | 1 | |
| VALFORO | 0 | 1 | 0 | 1 | |
| VELFORO | 0 | 11 | 0 | 11 | |
| VELFOURO | 0 | 1 | 0 | 1 | |
| VELPHON | 0 | 0 | 11 | 11 | |
| VELPHORE | 0 | 0 | 1 | 1 | |
| VELPHORO | 30 | 0 | 9 | 39 | |
| VELPHORU | 0 | 0 | 1 | 1 | |
| VELPHOW | 0 | 0 | 12 | 12 | |
| VELPHRO | 1 | 0 | 0 | 1 | |
| VELSFORO | 0 | 1 | 0 | 1 | |
| ZALFORO | 0 | 1 | 0 | 1 | |
| ZELFORO | 0 | 8 | 0 | 8 | |

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 Velphoro | Failure preventions |
|-----|------------------|--|------------------------|---|
| 1. | (b) (4) | | | |
| 2. | Zelboraf | Vemurafenib | Look | The pair has sufficient orthographic differences |
| 3. | Edurant | Rilpivirine Hydrochloride | Look | The pair has sufficient orthographic differences |
| 4. | Votrient | Pazopanib Hydrochloride | Look | The pair has sufficient orthographic differences |
| 5. | Valtropin | Somatropin Recombinant (rDNA origin) | Look | The pair has sufficient orthographic differences |
| 6. | Veletri | Epoprostenol Sodium | Look | The pair has sufficient orthographic differences |
| 7. | Valerian | Valeriana Officinalis | Look | The pair has sufficient orthographic differences |
| 8. | Naldecon | Chlor Pheniramine Maleate/ Phenylpropanolamine Hydrochloride/ Phenylephrine Hydrochloride/ Phenyltoloxamine citrate | Look | Naldecon has been discontinued since 2000. Unable to confirm accurate dosing information from commonly used drug databases. On December 22, 2005 the FDA issued a notice of proposed rulemaking (notice) for over-the-counter (OTC) nasal decongestant and weight control products containing phenylpropanolamine preparations. This proposed rule reclassifies phenylpropanolamine as non-monograph (Category II) not generally recognized as safe and effective. |
| 9. | Aquaphor | Petrolatum, Panthenol, Glycerin, Bisabolol | Sound | The pair has sufficient phonetic differences. |

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| No. | Proprietary Name | Active Ingredient | Similarity to Velphoro | Failure preventions |
|-----|------------------|--------------------------------|------------------------|--|
| 10. | Venlafaxine | Venlafaxine Hydrochloride | Sound | The pair has sufficient phonetic differences. |
| 11. | Valproate | Valproate Sodium | Sound | The pair has sufficient phonetic differences. |
| 12. | Venofer | Iron sucrose | Look & Sound | The pair has sufficient orthographic and phonetic differences. |
| 13. | Velcade | Bortezomib | Look & Sound | The pair has sufficient orthographic and phonetic differences. |
| 14. | Vitapro | Whey protein powder supplement | Look & Sound | The pair has sufficient orthographic and phonetic differences. |
| 15. | Velphoro | PA 21 | Look & Sound | Subject of this review |

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

| No. | Proposed name: Velphoro (PA 21) Dosage Form(s): Chewable Tablet Strength: 500 mg Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals. | Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple) | Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names |
|-----|---|--|---|
| 1. | Valproic acid (brand name is Depakene) 250 mg capsules and 250 mg/5 mL oral solution <u>Usual Dose:</u> <i>Complex Partial Seizures:</i> For adults and children 10 years of age or older. | Orthographic similarity -Both names begin with orthographically similar letter string 'Val vs. Vel', followed by identical downstroke letter 'p' and orthographically similar ending letter string since 'oic' can look like 'oro' Product characteristic similarity | Orthographic differences -The two names have different infixes since Valproic lacks the upstroke letter 'h' found in Velphoro -A typical prescription for Valproic acid would unlikely be written without the word "acid" which will help to further differentiate the two |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>Depakene has not been systematically studied as initial therapy. Patients should initiate therapy at 10 to 15 mg/kg/day. The dosage should be increased by 5 to 10 mg/kg/week to achieve optimal clinical response. Ordinarily, optimal clinical response is achieved at daily doses below 60 mg/kg/day.</p> <p><i>Simple and Complex Absence Seizures:</i></p> <p>The recommended initial dose is 15 mg/kg/day, increasing at one week intervals by 5 to 10 mg/kg/day until seizures are controlled or side effects preclude further increases. The maximum recommended dosage is 60 mg/kg/day. If the total daily dose exceeds 250 mg, it should be given in divided doses.</p> | <p>-Strength: Both products are single strength product that may be omitted on a prescription</p> <p>-Dose: Overlap in dose with Velphoro 1500 mg/day and Valproic acid 1500 mg/day (15 mg/kg/day for 100 kg adult) or dose of 6 caps/tabs per day</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are solid dosage forms (capsules vs. tablets)</p> | <p>names</p> |
| 2. | <p>Vilofane-DP 7.5 (Folic Acid)</p> <p>7.5 mg Tablets</p> <p><u>Usual Dose:</u> Medical food: 7.5 to 15 mg once daily</p> <p><u>Note:</u> Vilofane-DP 7.5 has been discontinued since 5/11/2011. Generic versions of folic acid is readily available on the market but not at the same 7.5 mg strength.</p> | <p>Orthographic similarity</p> <p>-Both names begin with orthographically similar letter string ‘Vil vs. Vel’, contain two upstroke letters (‘l’ and ‘f’ for Vilofane vs. ‘l’ and ‘h’ for Velphoro), and orthographically similar ending letter string since ‘ane’ can look like ‘oro’</p> <p>Product characteristic similarity</p> <p>-Strength: Both products are</p> | <p>Orthographic differences</p> <p>-The two names have different infixes since Vilofane-DP 7.5 lacks the downstroke/upstroke letter pair ‘ph’ found in Velphoro</p> <p>Product characteristic differences</p> <p>- Frequency of administration: Once daily vs. three times daily</p> |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>single strength product that may be omitted on a prescription</p> <p>-Dose: Both products can be ordered as ‘take 1 tablet’</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are tablets</p> | |
| 3. | <p>Veltane (Brompheniramine Maleate)</p> <p>4 mg Tablets</p> <p><u>Usual Dose:</u></p> <p>4 mg every 4 to 6 hr, not to exceed 24 mg/day.</p> | <p>Orthographic similarity</p> <p>-Both names begin with identical letter string ‘Vel’, contain two upstroke letters (‘l’ and ‘t’ for Veltane vs. ‘l’ and ‘h’ for Velphoro),, and orthographically similar ending letter string since ‘ane’ can look like ‘oro’</p> <p>Product characteristic similarity</p> <p>-Strength: Both products are single strength product that may be omitted on a prescription</p> <p>-Dose: Both products can be ordered as ‘take 1 tablet’</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are tablets</p> | <p>Orthographic differences</p> <p>-The two names have different infixes since Veltane lacks the downstroke letter ‘p’ between the two upstrokes found in Velphoro</p> |
| 4. | <p>Valturna (Aliskiren/Valsartan)</p> <p>Tablets</p> | <p>Orthographic similarity</p> <p>-Both names begin with</p> | <p>Orthographic differences</p> <p>-The two names have</p> |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>150 mg/160 mg and 300 mg/320 mg</p> <p><u>Usual Dose:</u></p> <p><i>Initial dosage:</i></p> <p>Aliskiren 150 mg/Valsartan 160 mg once daily.</p> <p><i>Dosage titration:</i></p> <p>May titrate up to Aliskiren 300 mg/ Valsartan 320 mg per day if blood pressure remains uncontrolled after 2 to 4 weeks.</p> <p><i>Maximum dose:</i></p> <p>Aliskiren 300 mg/Valsartan 320 mg per day.</p> <p><u>Note:</u> Valtorna has been discontinued since 7/20/2012. There are no Therapeutic Equivalents.</p> | <p>orthographically similar letter string ‘Val vs. Vel’, contain two upstroke letters (‘l’ and ‘t’ for Valtorna vs. ‘l’ and ‘h’ for Velphoro), and orthographically similar ending letter string since ‘na’ can look like ‘ro’</p> <p>Product characteristic similarity</p> <p>-Dose: Both products can be ordered as ‘take 1’</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are tablets</p> | <p>different infixes since Valtorna lacks the downstroke letter ‘p’ between the two upstrokes found in Velphoro</p> <p>Product characteristic differences</p> <p>-Strength: Velphoro is a single strength product so the strength may be omitted on a prescription but the strength for Valtorna must be specified and there is no overlap in the strength</p> <p>- Frequency of administration: Once daily vs. three times daily</p> |
| 5. | <p>Voltaren (Diclofenac Sodium)</p> <p>Extended-Release Tablet 100 mg</p> <p>Ophthalmic Solution 0.1%</p> <p>Gel 1%</p> <p><u>Usual Dose:</u></p> <p>For the relief of osteoarthritis, the recommended dosage is 100 mg</p> | <p>Orthographic similarity</p> <p>-Both names begin with orthographically similar letter string ‘Vol vs. Vel’ and contain two upstroke letters (‘l’ and ‘t’ for Voltaren vs. ‘l’ and ‘h’ for Velphoro)</p> <p>Product characteristic similarity</p> <p>-Strength/Dose: Both Voltaren</p> | <p>Orthographic differences</p> <p>-The two names have different infixes and suffixes since Voltaren lacks the downstroke letter ‘p’ between two upstrokes found in Velphoro. Additionally, the suffix for Voltaren is longer when scripted due to the additional ‘n’ at the end.</p> |

| No. | Proposed name: Velphoro (PA 21) Dosage Form(s): Chewable Tablet Strength: 500 mg Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals. | Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple) | Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names |
|-----|--|---|--|
| | <p>daily.</p> <p>For the relief of rheumatoid arthritis, the recommended dosage is 100 mg daily (the dose may be increased to 100 mg bid.)</p> <p><i>Cataract Surgery</i></p> <p>One drop of Voltaren Ophthalmic should be applied to the affected eye, 4 times daily beginning 24 hours after cataract surgery and continuing throughout the first 2 weeks of the postoperative period.</p> <p><i>Corneal Refractive Surgery</i></p> <p>One or two drops of Voltaren Ophthalmic should be applied to the operative eye within the hour prior to corneal refractive surgery. Within 15 minutes after surgery, one or two drops should be applied to the operative eye and continued 4 times daily for up to 3 days.</p> <p>Voltaren Gel should be measured onto the enclosed dosing card to the appropriate 2 g or 4 g designation. Lower extremities: Apply the gel (4 g) to the affected area 4 times daily</p> <p>Upper extremities: Apply the gel (2 g) to the affected area 4 times daily</p> | <p>and Velphoro can be written without the strength as “take 1 tab”</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are available as tablets</p> | |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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> |
|-----|--|--|--|
| 6. | <p>Valtrex (Valacyclovir Hydrochloride) Caplets</p> <p>500 mg and 1 gm</p> <p><u>Usual Dose:</u></p> <p><i>Cold Sores (Herpes Labialis):</i> The recommended dosage for treatment of cold sores is 2 grams twice daily for 1 day taken 12 hours apart. Therapy should be initiated at the earliest symptom of a cold sore (e.g., tingling, itching, or burning).</p> <p><i>Genital Herpes:</i></p> <p><i>Initial Episode:</i> The recommended dosage for treatment of initial genital herpes is 1 gram twice daily for 10 days. Therapy was most effective when administered within 48 hours of the onset of signs and symptoms.</p> <p><i>Recurrent Episodes:</i> The recommended dosage for treatment of recurrent genital herpes is 500 mg twice daily for 3 days. Initiate treatment at the first sign or symptom of an episode.</p> <p><i>Suppressive Therapy:</i> The recommended dosage for chronic suppressive therapy of recurrent genital herpes is 1 gram once daily in patients with normal immune function. In patients with a history of 9 or fewer recurrences per year, an</p> | <p>Orthographic similarity</p> <p>-Both names begin with orthographically similar letter string ‘Val vs. Vel’, contain two upstroke letters (‘l’ and ‘t’ for Valtrex vs. ‘l’ and ‘h’ for Velphoro)</p> <p>Product characteristic similarity</p> <p>-Strength: Both products share overlapping strengths (500 mg)</p> <p>-Dose: Both products can be ordered as 1 tab, 1 g, or 1000 mg</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are solid oral dosage forms</p> <p>-Frequency of administration: Both products are administered three times a day</p> | <p>Orthographic differences</p> <p>-The two names have different infixes/suffixes since Valtrex lacks the downstroke letter ‘p’ between two upstrokes found in Velphoro and the letter strings at the end of the names appear different when scripted (‘rex’ vs. ‘oro’)</p> |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>alternative dose is 500 mg once daily.</p> <p>In HIV-1 infected patients with a CD4+ cell count greater than or equal to 100 cells/mm³, the recommended dosage for chronic suppressive therapy of recurrent genital herpes is 500 mg twice daily.</p> <p><i>Reduction of Transmission:</i> The recommended dosage for reduction of transmission of genital herpes in patients with a history of 9 or fewer recurrences per year is 500 mg once daily for the source partner.</p> <p><i>Herpes Zoster:</i> The recommended dosage for treatment of herpes zoster is 1 gram 3 times daily for 7 days. Therapy should be initiated at the earliest sign or symptom of herpes zoster and is most effective when started within 48 hours of the onset of rash</p> <p><i>Cold Sores (Herpes Labialis):</i> The recommended dosage for the treatment of cold sores in pediatric patients aged greater than or equal to 12 years is 2 grams twice daily for 1 day taken 12 hours apart. Therapy should be initiated at the earliest symptom of a cold sore (e.g., tingling, itching, or burning).</p> <p><i>Chickenpox:</i> The recommended dosage for treatment of chickenpox in</p> | | |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>immunocompetent pediatric patients aged 2 to less than 18 years is 20 mg/kg administered 3 times daily for 5 days. The total dose should not exceed 1 gram 3 times daily. Therapy should be initiated at the earliest sign or symptom.</p> | | |
| 7. | <p>Vol-Plus (Ascorbic Acid (Vitamin C) 120 mg, Beta-Carotene (Vitamin A) , Calcium 200 mg [Calcium Sulfate], Cholecalciferol 400 IU, Copper 2 mg [Copper Oxide] [Cupric Oxide], Cyanocobalamin (Vitamin B12) 12 mcg, D₁-Alpha Tocopheryl Acetate (Vitamin E) 22 mg, Folic Acid (Vitamin B9) 1 mg, Iron 27 mg [Ferrous Fumarate], Niacinamide 20 mg, Pyridoxine (Vitamin B6) 10 mg, Riboflavin (Vitamin B2) 3 mg, Thiamine Mononitrate (Vitamin B1) 1.84 mg, Vitamin A 4000 IU, Vitamin A Acetate , Zinc 25 mg [Zinc Oxide]) Tablet</p> <p><u>Usual Dose:</u> Take one daily.</p> | <p>Orthographic similarity -Both names begin with orthographically similar letter string ‘Vol vs. Vel’, followed by identical downstroke letter ‘p’ and adjacent to an upstroke letter (‘l vs. h’)</p> <p>Product characteristic similarity -Strength: Both products are single strength product so strength may be omitted on a prescription -Dose: Both products can be ordered as ‘take 1’ -Route of administration: Both products are orally administered -Dosage formulation: Both products are available as tablets</p> | <p>Orthographic differences - Velphoro has an additional ‘o’ at the end of the name, giving the suffixes a different appearance when scripted(from ‘us’ vs. ‘oro’)</p> <p>Product characteristic differences - Frequency of administration: Once daily vs. three times daily</p> |
| 8. | | | |

(b) (4)

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| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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> |
|-----|---|---|--|
| | (b) (4) | | |
| 9. | <p>Zelapar (Selegiline Hydrochloride) Orally Disintegrating Tablet (ODT) 1.25mg</p> <p><u>Usual Dose:</u></p> <p>Treatment should be initiated with 1.25 mg given once a day for at least 6 weeks. After 6 weeks, the dose may be escalated to 2.5 mg given once a day if a desired benefit has not been achieved and the patient is tolerating</p> | <p>Orthographic similarity -Both names begin with orthographically similar letter ‘Z vs. V’, followed by identical letter string ‘el’, and both names contain the identical downstroke letter ‘p’</p> <p>Product characteristic similarity -Strength: Both products are single strength product that may be omitted on a prescription</p> | <p>Orthographic differences -The two names have different infixes/ suffixes due to the vowel ‘a’ separating the upstroke letter ‘l’ and the downstroke letter ‘p’ in Zelapar. Additionally, Zelapar lacks a second upstroke letter unlike Velphoro with the ‘h’ (‘apar’ vs. ‘phoro’)</p> <p>Product characteristic</p> |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>it. There is no evidence that doses greater than 2.5 mg a day confer any additional benefit, and they should ordinarily be avoided because of the potential increased risk of adverse events.</p> | <p>-Dose: Both products can be ordered as ‘take 1’</p> <p>-Route of administration: Both products are orally administered (albeit ODT vs. chewable)</p> | <p>differences</p> <p>-Frequency of administration: once daily vs. three times a day</p> |
| 10. | <p>Relpax (Eletriptan) Tablets</p> <p>20 mg and 40 mg</p> <p><u>Usual Dose:</u></p> <p>Single doses of 20 mg and 40 mg were effective for the acute treatment of migraine in adults (maximum recommended single dose is 40 mg). If a second dose is required, it should be taken at least 2 hours after the initial dose. The maximum daily dose should not exceed 80 mg.</p> | <p>Orthographic similarity</p> <p>-Both names begin with orthographically similar letter ‘R vs. V’, followed by identical letter string ‘el’, and contain identical downstroke letter ‘p’ in the same 4th position</p> <p>Phonetic similarity</p> <p>-Both names begin with phonetically similar beginning syllable from the sounds of ‘Rel vs. Vel’</p> <p>Product characteristic similarity</p> <p>-Dose: Both products can be ordered as ‘take 1’</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are available as tablets</p> | <p>Orthographic differences</p> <p>-The two names have different infixes/ suffixes due to the extra ending vowel ‘o’ and a second upstroke letter ‘h’ in Velphoro (‘ax’ vs. ‘horo’)</p> <p>Phonetic differences</p> <p>-Relpax has only two syllables while Velphoro has 3 syllables with distinctive second and third syllables from the sound of ‘pax’ vs. ‘pho’ and ‘ro’</p> <p>Product characteristic differences</p> <p>-Strength: Velphoro is a single strength product so the strength may be omitted on a prescription but Relpax is a multiple strength product so the strength must be specified and there is no overlap in the strength</p> <p>-Frequency of administration: single dose (or repeat in 2</p> |

| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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>hours after first dose if needed) vs. three times a day</p> |
| 11. | <p>Zohydro ER^{***} (Hydrocodone Bitartrate) Extended-Release Capsule 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p><u>Usual Dose:</u> Dose is titrated based upon pain level and opioid tolerance with a frequency of every 12 hours</p> <p><u>Note:</u> Zohydro ER name was found acceptable in review OSE RCM #2012-1388 dated September 12, 2012 under NDA 202880.</p> | <p>Orthographic similarity -Both names begin with orthographically similar letter string ‘Zo vs. Ve’, contain two upstroke letters (‘h’ and ‘d’ for Zohydro vs. ‘l’ and ‘h’ for Velphoro), one downstroke letter (‘y’ vs. ‘p’), and end with identical letter string ‘ro’</p> <p>Phonetic similarity -Both names have 3 syllables and end with phonetically similar sounds of ‘roh’</p> <p>Product characteristic similarity -Strength: Both products share numerical similarity in strengths (500 mg vs. 50 mg) -Dose: Both products can have overlap if ordered as ‘take 1’ or 500 mg vs. 50 mg -Route of administration: Both products are orally administered -Dosage formulation: Both</p> | <p>Orthographic differences -The shapes of the two names are different due to the shapes of the upstroke and downstroke letters when scripted (‘h’ vs. ‘l’, ‘y’ vs. ‘p’, and ‘d’ vs. ‘h’) and the addition of the vowel ‘o’ which elongates the suffix of the Velphoro name compared to Zohydro.</p> <p>-The modifier ‘ER’ in the Zohydro name when included will provide additional orthographic differentiation from Velphoro</p> <p>Phonetic differences -Zohydro and Velphoro have distinctive second and third syllables from the sound of ‘Zo’ vs. ‘Vel’ and ‘hy’ vs. ‘pho’</p> |

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| No. | <p>Proposed name: Velphoro (PA 21)</p> <p>Dosage Form(s): Chewable Tablet</p> <p>Strength: 500 mg</p> <p>Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals.</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> |
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| | | <p>products are solid oral dosage forms</p> | |
| 12. | <p>Tylenol (Acetaminophen)</p> <p>650 mg Caplets (Take 2 caplets every 8 hours)</p> <p>500 mg Gelcaps and Caplets (Take 2 caplets or gelcaps every 6 hours)</p> <p>325 mg Tablets (Take 2 tablets every 4 hours to 6 hours)</p> <p><u>Usual Dose:</u> Take “2” every 4 hours, 6 hours, or 8 hours depending on the strength as noted above.</p> | <p>Orthographic similarity -Both names contain identical upstroke letter ‘l’ in the 3rd position of the name</p> <p>Product characteristic similarity -Strength: Both products have overlapping strengths (500 mg)</p> <p>-Dose: Both products can have overlap in doses if ordered as ‘take 2’ or 1000 mg (since Velphoro dose maybe increased by 500 mg per day as needed).</p> <p>-Route of administration: Both products are orally administered</p> <p>-Dosage formulation: Both products are tablets</p> <p>-Frequency of administration: Both products are administered three times daily</p> | <p>Orthographic differences (b) (4)</p> <p>Tylenol differs from Velphoro in the shape and length due to differing letter strings, upstroke and downstroke letters resulting in different prefixes (from ‘Ty’ vs. ‘Ve’), infixes (from ‘en’ vs. ‘pho’), and suffixes (from ‘ol’ vs. ‘ro’)</p> |
| 13. | <p>Valchlor (Mechlorethamine HCl) Gel 0.02%</p> <p><u>Usual Dose:</u> Apply a thin layer of gel topically to affected area(s) once daily.</p> | <p>Phonetic similarity -Both names have phonetically similar beginning syllable with the sounds from ‘Val’ vs. ‘Vel’ and similar second syllable from the sound of ‘or’ in ‘chlor’ and ‘phor’</p> | <p>Phonetic differences -Valchlor has 2 syllables while Velphoro has 3 syllables and Valchlor has phonetic distinction from Velphoro due to the hard ‘c’ sound in ‘chlor’ vs. the soft ‘f’ sound in ‘phor’</p> |

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| No. | Proposed name: Velphoro (PA 21) Dosage Form(s): Chewable Tablet Strength: 500 mg Usual Dose: 1500 mg/day (one 500 mg tablet tid with meals). Increase or decrease by 500 mg per day as needed. Max dose 3000 mg or total 6 tablets per day in divided doses three times daily with meals. | Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple) | Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names |
| | | Product characteristic similarity -Strength: Both products are single strength product that may be omitted on a prescription | Product characteristic differences -Frequency of administration: once daily vs. three times daily with meals -Dose: No overlap in dose (thin layer vs. X tablet(s) or 500 mg to 1000 mg) |

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/s/

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