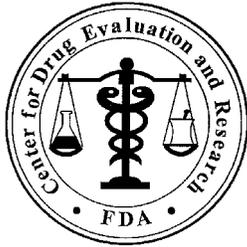


CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:
22511Orig1s000**

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: April 14, 2010

To: Donna Griebel, MD, Director
Division of Gastroenterology Products

Through: Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Laura Pincock, Pharm.D., Acting Team Leader
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Vimovo (Naproxen and Esomeprazole Magnesium) Tablets
375 mg/20 mg and 500 mg/20 mg

Application Type/Number: NDA 022511

Applicant: Pozen, Inc.

OSE RCM #: 2009-1779

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1 INTRODUCTION

This re-assessment of the proposed proprietary name Vimovo 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, Vimovo, acceptable in OSE Review # 2009-1244 dated September 10, 2009. In addition, the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective, and the Division of Gastroenterology Products did not have any concerns with the proposed proprietary name, Vimovo, during our initial review.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We used the same search criteria previously used in OSE Review #2009-1244. Because none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems that may have been added during any USAN updates that occur since the initial 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 proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases referenced in Section 4 did not yield any new names thought to look or sound similar to Vimovo and represent a potential source of drug name confusion. Likewise, DMEPA staff did not identify any USAN stems in the proposed proprietary name Vimovo as of April 8, 2010. Accordingly, DMEPA finds the proposed proprietary name Vimovo acceptable for this product.

3 CONCLUSIONS AND RECOMMENDATIONS

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

DMEPA considers this a final proprietary name review. However, if approval of the NDA is delayed beyond 90 days from the date of this review, DGP should notify DMEPA because the proposed proprietary name must be re-reviewed prior to the new approval date.

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

4 REFERENCES

1. OSE Review # 2009-1244 dated September 10, 2009. Proprietary Name Review of Vimovo (Naproxen and Esomeprazole Magnesium) Tablets. Raichell S. Brown, Safety Evaluator.

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/ama1/pub/upload/mm/365/stem-list-cumulative.pdf>)

USAN Stems List contains all the recognized USAN stems.

4. *CDER Proposed Names List*

CDER Proposed Names List is a compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

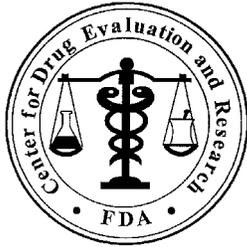
Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22511	ORIG-1	POZEN INC	PN 400 NAPROXEN/ESOMEPRAZOLE MAGNESIUM

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

/s/

LAURA L PINCOCK
04/15/2010

DENISE P TOYER
04/15/2010



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date: September 10, 2009

To: Donna Griebel, MD, Director
Division of Gastroenterology Products

Through: Laura Pincock Pharm.D., Acting Team Leader
Kellie Taylor, Pharm.D., MPH, Team Leader
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Division of Medication Error Prevention and Analysis (DMEPA)

From: Raichell Brown, Pharm.D., J.D., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Vimovo (Naproxen and Esomeprazole Magnesium) Tablets
375 mg/20 mg and 500 mg/20 mg

Application Type/Number: NDA 22-511

Applicant: Pozen Inc.

OSE RCM #: 2009-1244

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EXECUTIVE SUMMARY

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

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Pozen, Inc. dated June 30, 2009 for an assessment of the proposed proprietary name, Vimovo, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. In addition, the Applicant submitted an external study in support of their proposed proprietary name.

Pozen Inc. also submitted container labels and carton labeling for review. The labels and labeling will be reviewed separately under OSE Review #2009-1245.

1.2 REGULATORY HISTORY

DMEPA reviewed and had no objection to the proposed proprietary name (b) (4) for this product on December 5, 2008 (see OSE Review # 2007-2558 for IND# 76,301). However, the Applicant submitted a Request for Proprietary Name Review for Vimovo on June 30, 2009 stating that the tradename (b) (4) cannot be used for this product “due to language issues in other parts of the world.”

1.3 PRODUCT INFORMATION

Vimovo (Naproxen/Esomeprazole Magnesium) Tablets are indicated for relief of signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in patients at risk of developing NSAID-associated gastric ulcers.

Vimovo will be available in two strengths, 375 mg/20 mg and 500 mg/20 mg. The recommended dose is one tablet taken orally twice daily. Vimovo should be taken 30 minutes before meals. The Naproxen component of Vimovo is enteric coated. The tablets should be swallowed whole and should not be split, chewed, or crushed.

Dose reductions are recommended, with regard to the Naproxen component, in patients with mild to moderate hepatic impairment. Vimovo is not recommended for patients with severe liver impairment because these patients should not receive more than 20 mg of Esomeprazole per day.

Likewise, Vimovo is not recommended in patients with moderate to severe renal impairment (i.e. creatinine clearance less than 30 mL/minute) because of the Naproxen component.

The tablets will be packaged in bottles containing 60 tablets and 500 tablets, as well as in boxes of unit dose blister packs containing 100 tablets. Vimovo tablets should be stored at room temperature.

Vimovo has a Medication Guide for Non-Steroidal Anti-Inflammatory Drugs (NSAIDS).

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to Vimovo, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (one, capital letter ‘V’), down strokes (none), cross strokes (none), and dotted letters (none). Additionally, some letters in Vimovo may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Vimovo.

When searching to identify potential names that may sound similar to Vimovo, the DMEPA staff searches for names with similar number of syllables (three), stresses (VI-mo-vo, vi-MO-vo, or vi-mo-VO), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary. For example, ‘Vi-’ may sound like ‘Ve-’, ‘Va-’, ‘Vo-’, ‘Bi-’, ‘Bye-’ or ‘Bee’. Likewise, ‘-movo’ may sound like ‘-mova’, ‘-muvo’, ‘-novo’, or ‘-nova’. (Also see Appendix B).

The Applicant did not supply the intended pronunciation for this name and thus it could not be considered. Nevertheless, names are often mispronounced and/or spoken with regional accents and dialects, so multiple potential pronunciations of the name are considered.

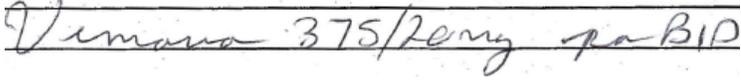
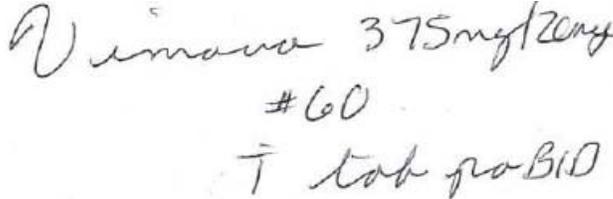
¹ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

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

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Vimovo Study (conducted on July 27, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Vimova 375 mg/20 mg Take 1 tablet by mouth twice daily Dispense # 60</p>
<p><u>Outpatient Prescription:</u></p> 	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name conducted by (b) (4), a subsidiary of (b) (4). The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of his/her overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 18 names as having some similarity to the name Vimovo.

Seventeen of the names were thought to look like Vimovo. These include: Innovar, (b) (4), Lunivia***, Nexavar, (b) (4), Remeron, Vascana***, Vermox, Vimar, Vimax, Vimpat, (b) (4), Viramune, Visacor, Vivarin, (b) (4), and Vumon. One name, Renova, was thought to both look and sound like Vimovo.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of August 10, 2009.

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-four practitioners responded with none of the responses overlapping with an existing name. None of the participants interpreted the name correctly as “Vimovo.” In both inpatient and outpatients studies the ‘i’ in Vimovo was misinterpreted as ‘e’, the second ‘v’ was misinterpreted as ‘n’ or ‘r’, and the ‘o’ in both positions were misinterpreted as ‘a’. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Vimovo. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL NAME STUDY

In the proposed name risk assessment submitted by the Applicant, (b) (4) identified and evaluated a total of 22 names thought to have some potential for confusion with the name Vimovo. The names are Bismuth, Darvon, Feosol, Nimotop, Quetiapine, Renova, Rimso, Timolol, Valproate, Vanadom, Vantin, Velosef, Vermox, Viagra, Vigamox, Vimpat, Vioxx, Vivotif, Vumon, Zymar, Zymine, and Zyvox. Of the 22 names identified by (b) (4) 5 were also identified by DMEPA during the database searches: Renova, Rimso, Vermox, Vimpat, and Vumon. The remaining 17 names were evaluated as part of the Safety Evaluator Risk Assessment.

3.5 COMMENTS FROM THE DIVISION OF GASTROENTEROLOGY PRODUCTS (DGP)

DMEPA notified the Division of Gastroenterology Products via e-mail that we had no objections to the proposed proprietary name, Vimovo, on August 5, 2009. Per e-mail correspondence, the Division of Gastroenterology Products on August 7, 2009 indicated that they concur with our assessment of the proposed proprietary name, Vimovo.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in one additional name which was thought to look or sound similar to Vimovo and represent a potential source of drug name confusion. The name identified to have look-alike and sound-alike similarities was Rimso-50.

Accordingly, we evaluated a total of 36 names: 18 identified in Database and Information Sources (Section 3.1), 17 identified in the External Study (Section 3.4), and 1 identified in this section by the primary Safety Evaluator.

4 DISCUSSION

DDMAC and the Review Division had no concerns with the proposed proprietary name, Vimovo. DMEPA did not identify and safety issues with the proposed product except for potential orthographic and/or phonetic similarity with other drug names.

DMEPA identified and evaluated 36 names for their potential similarity to the proposed name, Vimovo. Twenty-nine lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 7 names and lead to medication errors. This analysis determined that the name similarity between Vimovo was unlikely to result in medication errors with any of the 7 products for the reasons presented in Appendices E through G. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Vimovo, is not vulnerable to name confusion that could lead to medication errors nor is it promotional. Our assessment supports the findings of the External Study submitted by the Applicant. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Vimovo for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

If you have further questions or need clarifications, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

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

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

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

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

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

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

4. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

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

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

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

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

7. *Electronic online version of the FDA Orange Book* (<http://www.fda.gov/cder/ob/default.htm>)

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

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

USPTO provides information regarding patent and trademarks.

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

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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

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

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

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

³ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to: established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁵ DMEPA provides the product characteristics considered for this review in Section 1.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly, and even dissimilarly, spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted are in Table 1 below. In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

⁵ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	<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 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, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff 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, the DMEPA staff 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.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed name.

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwritten and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written; each consists of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

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

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys its decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section 1. 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, prescription studies, and external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names 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.

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or

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

suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant 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. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission (TJC), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant 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. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant 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 Applicants have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Vimovo	Scripted may appear as	Spoken may be interpreted as
Capital 'V'	i, l, U, u, N, n, Y or Z	Bb, Rr
Lower case 'v'	u, r, or n,	
Lower case 'i'	e or l	a, e, ee, ey, y, o, u
Lower case 'm'	n, 'rr' or u	n
Lower case 'im'	'irn', 'em' or 'ur'	
Lower case 'o'	a, u, 'ri', 're'	a, 'oh'

Appendix C: FDA Prescription Study Responses (conducted July 27, 2009).

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Vemana	Vimana	Benova
Vemarra	Vimara	Vemohah
Vemarva	Vimova	Vemova
Vimana	Vimova	Vemova
Vimara	Vimova	Vemova
Vimaria		Venova
Vimaria		Vimova
Vimarra		Vimova
Vimarra		Vimova
Vimava		

Appendix D: Names Lacking Orthographic and/or Phonetic Similarity to Vimovo.

Name	Name
Innovar	Nimotop
Lunivia***	Quetiapine
Nexavar	Timolol
Vascana***	Valproate
Vermox	Vanadom
Vimax	Vantin
Vimpat	Velosef
(b) (4)	Viagra
Viramune	Vigamox
Visacor	Vioxx
Vivarin	Vivotif
(b) (4)	Zymar
Bismuth	Zymine
Darvon	Zyvox
Feosol	

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

Appendix E: Drug names that are not currently marketed in the U.S.

Proprietary Name	Similarity to Vimovo	Status
(b) (4)		
(b) (4)		

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

Appendix F: Products with no numerical overlap or similarity in strength or dosing interval.

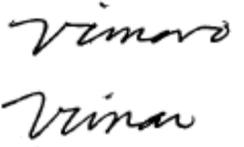
Product name with potential for confusion	Similarity to Vimovo	Strength	Usual Dose
Vimovo (Naproxen/ Esomeprazole magnesium) Tablet	N/A	375 mg/20 mg, 500 mg/20 mg	One tablet by mouth twice a day 30 minutes before meals.
Remeron (Mirtazapine)	orthographic	Tablet and Orally Disintegrating Tablet: 15 mg, 30 mg, and 45 mg	15 mg, 30 mg, or 45 mg by mouth once a day.
Renova (Tretinoin)	orthographic and phonetic	Topical Cream: 0.02% and 0.05%	Apply a pea-size amount of cream to entire face once a day in the evening.

Appendix G: Products with similarity in strength or dose with multiple differentiating product characteristics.

Product name with potential for confusion	Similarity to Vimovo	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Vimovo vs. Rimso-50)
Vimovo (Naproxen/ Esomeprazole magnesium) Tablet	N/A	375 mg/20 mg, 500 mg/20 mg	One tablet by mouth twice a day 30 minutes before meals	N/A
Rimso-50 (Dimethyl Sulfoxide) Intravesical Solution	orthographic	50%	Instill 50 mL into bladder via catheter or syringe; allow to remain for 15 minutes before voiding. Repeat at 14-day intervals until symptomatic relief attained.	<p><u>DOSAGE FORM:</u> Vimovo is an oral tablet. Rimso-50 is an intravesical solution.</p> <p><u>ROUTE OF ADMINISTRATION:</u> Vimovo is administered orally. Rimso-50 is administered intravesically, directly into the bladder via a catheter or syringe.</p> <p><u>RECOMMENDED DOSE:</u> Vimovo is dosed as one tablet, 375 mg/20mg, or 500 mg/20 mg. Rimso-50 is dosed as 50 mL.</p> <p><u>FREQUENCY OF ADMINISTRATION:</u> Vimovo is administered twice daily. Rimso-50 is administered no more frequently than once every two weeks.</p> <p><u>INDICATION FOR USE:</u> Vimovo is indicated for anti-inflammatory therapy in patients at risk for developing NSAID-induced gastric ulcers. Rimso-50 is indicated for symptomatic relief of interstitial cystitis.</p>

Product name with potential for confusion	Similarity to Vimovo	Strength	Usual Dose (if applicable)	Differentiating Product Characteristics (Vimovo vs. Rimso-50)
Vimovo (Naproxen/ Esomeprazole magnesium) Tablet	N/A	375 mg/20 mg, 500 mg/20 mg	One tablet by mouth twice a day 30 minutes before meals	N/A
Vumon (Teniposide) Intravenous Solution	orthographic	10 mg/mL	165 mg/m ² intravenously twice a week for 8 to 9 doses or 250 mg/m ² intravenously once weekly for 4 to 8 weeks <u>Examples:</u> 165 mg/m ² x 2.2 m ² = 375 mg dose 250 mg/m ² x 1.5 m ² = 375 mg dose 250 mg/m ² x 2 m ² = 375 mg dose	<u>DOSAGE FORM:</u> Vimovo is an oral tablet. Vumon is an intravenous solution. <u>ROUTE OF ADMINISTRATION:</u> Vimovo is administered orally. Vumon is administered intravenously. <u>FREQUENCY OF ADMINISTRATION:</u> Vimovo is administered twice daily. Vumon is administered once or twice a week. <u>SETTING OF USE:</u> Vimovo is a drug for both inpatient and out patient use. Vumon is administered by a health care professional and likely to be ordered on a chemotherapy order form. Additionally, Vumon, is labeled and stored as a cytotoxic agent. <u>INDICATION FOR USE:</u> Vimovo is indicated for anti-inflammatory therapy in patients at risk for developing NSAID-induced gastric ulcers. Vumon is indicated for refractory Acute Lymphoid Leukemia, in combination with other agents.

Appendix H: Potential confusing name with overlap in numerical strength or dose.

Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>Vimovo (Naproxen/ Esomeprazole magnesium) 375 mg/20 mg, 500 mg/20 mg Tablets</p>		<p>Medication errors are unlikely to occur due to differences in proposed product characteristics.</p>
<p>Vimar (multivitamin) Oral Drops</p>	<p>Orthographic Similarities:</p> <p>Both tradenames begin with <i>Vim-</i></p> <p>The endings of each name, <i>-ovo</i> and <i>-ar</i> are indistinguishable when scripted</p> <p><u>Ex.</u></p>  <p>Numerical Overlap in Dose:</p> <p>Both products will have a dose of 'One' (i.e. One tablet and One Dropperful)</p>	<p>Certain factors that define the usual practice settings for each product reduces the likelihood of medication errors in the usual practice setting.</p> <p>Rationale:</p> <p><i>Vimovo one tablet by mouth twice daily</i> is unlikely to be mistaken for <i>Vimar one dropperful by mouth once daily</i>, or vice-versa. Although both tradenames are orthographically similar because the first three letters of each name are identical and the letters in the end of each name appear similar when scripted, the proposed name Vimovo appears notably longer than the tradename Vimar when the tradenames are scripted.</p> <p>In addition, factors that define the “usual practice setting” for use of Vimovo and Vimar decrease the likelihood of confusion between these products. Vimovo is a prescription product; on the other hand, Vimar is an over-the-counter product. Additionally, prescribers are likely to use the word ‘dropperful’ (or some related variation of the word) in the prescription order on a prescription for Vimar. Use of the word ‘dropperful’ on a prescription for Vimar is distinguishing information. Lastly, Vimovo will be available in two strengths, 375 mg/20 mg and 500 mg/20 mg. Therefore, a prescriber of Vimovo must indicate the strength on a prescription order.</p>

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