CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204516Orig1s000

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:	April 22, 2013
Reviewer:	Manizheh Siahpoushan, PharmD Division of Medication Error Prevention and Analysis
Acting Team Leader:	James Schlick, RPh, MBA Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Brisdelle (Paroxetine) Capsules, 7.5 mg
Application Type/Number:	NDA 204516
Applicant/sponsor:	Noven Therapeutics
OSE RCM #:	2013-859

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

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Brisdelle 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, Brisdelle, acceptable in OSE Review #2012-2990 dated March 14, 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 #2012-2990. 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 one new name, (Minivelle), thought to look similar to Brisdelle and represent a potential source of drug name confusion. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Minivelle and lead to medication errors. This analysis determined that the name similarity between Brisdelle and the identified name was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the 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 United States Adopted Names (USAN) stems in the proposed proprietary name as of April 16, 2013. The Office of Prescription Drug Promotion (OPDP) had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Brisdelle, did not identify any vulnerability that would result in medication errors with any additional name noted in this review. Thus, DMEPA has no objection to the proprietary name, Brisdelle, 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 Reproductive and Urologic Products 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 Marcus Cato, OSE project manager, at 301-796-3903.

4 REFERENCES

1. OSE Review #2012-2990, Brisdelle (Paroxetine) Proprietary Name Review, Siahpoushan, M. March 14, 2013.

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.

Appendix A: 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.	**Proprietary name: Brisdelle (Paroxetine)** **Dosage form: Capsules** **Strength:7.5 mg** **Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime**	**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.	Minivelle (Estradiol) Transdermal System 0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, 0.1 mg per 24 hours Usual Dose: Apply one patch twice weekly.	Orthographic: Both names consist of nine letters, share the ending letter string '-elle', beginning letters that may appear similar when scripted ('B' vs. 'M') followed by letter strings that may be difficult to differentiate when scripted in cursive font ('-ris-' vs. '-ini-'). Additionally, the letter 'd' in Brisdelle may appear similar to the letter 'v' in Minivelle specially if the letter 'd' is not fully closed or fully extended. Partial Overlap in the Usual Dose: One (tablet vs. patch)	Strength: Single strength (7.5 mg) vs. multiple strengths (0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, and 0.1 mg) with no overlap between the strengths. Frequency of administration: Once daily vs. twice weekly

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/s/

MANIZHEH SIAHPOUSHAN
04/22/2013

JAMES H SCHLICK
04/22/2013

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:	March 14, 2013
Reviewer:	Manizheh Siahpoushan, PharmD Division of Medication Error Prevention and Analysis
Team Leader:	Zachary Oleszczuk, PharmD Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Brisdelle (Paroxetine) Capsules, 7.5 mg
Application Type/Number:	NDA 204516
Applicant/Applicant:	Noven Therapeutics, LLC
OSE RCM #:	2012-2990

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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Brisdelle, 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 BACKGROUND AND REGULATORY HISTORY

The Applicant submitted a request for proprietary name review of Brisdelle (Paroxetine), NDA 204516 on December 26, 2012. This is the fifth proposed proprietary name submitted for this product. The first four names were submitted, and reviewed by DMEPA under IND 076636.

The first proposed propriety name Mesafem***, submitted for review on July 8, 2010 was found unacceptable in OSE Review #2010-1620, dated January 5, 2011, for potential confusion between the proposed name and Sarafem because of orthographic and product characteristic similarities.

The second proposed proprietary name (b) (4) submitted for review on March 30, 2011 was found unacceptable in OSE Review #2011-1188, dated September 21, 2011, for potential confusion between the proposed name and (b) (4) because of orthographic and product characteristic similarities.

The third proposed proprietary name (b) (4) submitted for review on February 21, 2012 was found unacceptable in OSE Review #2012-485, dated March 20, 2012, due to the proposed proprietary name misleadingly overstating the efficacy of the product.

The fourth proposed proporietary name (b) (4) submitted for review on June 8, 2012 was found unacceptable in OSE Review #2012-1376, dated November 27, 2012, for potential confusion between the proposed name and (b) (4)

Noven Therapeutics also markets the active ingredient, Paroxetine Mesylate, under the proprietary name, Pexeva. Pexeva was approved by the FDA on July 3, 2003, under NDA 021299. For this application, the Applicant is proposing a new strength of Paroxetine to be marketed under the proprietary name, Brisdelle. However, the Applicant did not provide any rational for using a dual proprietary name in their submission for the proposed proprietary name, Brisdelle.

As the Applicant is proposing a new strength of Paroxetine under a new name, a discussion of dual proprietary names was previously addressed in OSE review #2010-1620 when this product was submitted with the proposed proprietary name Mesafem.*** At that time, the use of a dual proprietary name was found acceptable as neither DRUP nor DPP expressed safety concerns with the Applicant's proposal to use dual proprietary names, and the risk of concomitant therapy already existed because Paxil (Paroxetine HCl), the generic equivalents of Paxil, and Pexeva (Paroxetine Mesylate) were currently on the market together. Dual proprietary names were not discussed in OSE review #2011-1188 ((b) (4) or OSE review #2012-485 ((b) (4) OSE Review #2012-1376, dated November 27, 2012 (section 2.2.6 Failure Mode and Effects

Analysis of Similar Names) includes the latest detailed discussion of the dual proprietary names (Appendix F), where a dual proprietary name was once again found acceptable. Therefore, we will not discuss dual proprietary names in this review because we continue to find them acceptable for this product.

OSE Review #2012-1376, dated November 27, 2012, also includes an updated search of the FDA Adverse Event Reporting System for medication errors involving Prozac and Sarafem because this dual proprietary name exists and is similar to Pexeva and Brisdelle, specifically searched for patients who may have been prescribed both Prozac and Sarafem at the same time. Prozac and Sarafem are dual proprietary names for Fluoxetine Hydrochloride, and both owned by Eli Lily and Co. In addition, medication errors involving Pexeva (Paroxetine Mesylate) and Paxil (Paroxetine Hydrochloride) were also searched, specifically looking to see if patients were being prescribed both Pexeva and Paxil at the same time. Therefore an updated search of the FDA Adverse Event Reporting System for medication error cases was not conducted for this review. See appendix F (section 2.2.3 Medication Error Data Selection of Cases) for the search results and an assessment of the cases.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 26, 2012 proprietary name submission.

- Active Ingredient: Paroxetine
- Indication of Use: Treatment of moderate to severe vasomotor symptoms associated with menopause
- Route of Administration: Oral
- Dosage Form: Capsules
- Strength: 7.5 mg
- Dose and Frequency: One capsule once daily at bedtime
- How Supplied: [redacted] (b) (4) blister packs of 30 capsules. Professional samples of 7 capsules [redacted] (b) (4) blister packs will also be available.
- Storage: Room Temperature
- Container and Closure Systems: The commercial packaging for the capsules consists of [redacted] (b) (4) blister packets. [redacted] (b) (4)

2 RESULTS

The following sections provide the 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 Reproductive and Urologic Products 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 January 3, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Brisdelle, is a 'blank canvas'. 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

Thirty-five practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Nine out of thirty-five participants interpreted the name correctly as Brisdelle (seven inpatient and two outpatient participants). Eleven voice prescription studies misinterpreted the name incorrectly as: Breystil, Brisdale, Brisdel, Brisdell, Brisdow, Brisdyl, Bristel, Bristow, and Brizdel. Six participants in the outpatient prescription studies misinterpreted the ending letter string '-el' as '-ec'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, January 8, 2013 e-mail, the Division of Reproductive and Urologic Products (DRUP) 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 of Similar Names

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

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)					
Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Brilinta	EPD	Brevital	EPD	Tridil	EPD
Brevibloc	EPD	Brickellia	EPD	Brondelate	EPD
Brintellix***	EPD	(b) (4)	PR	Baraclude	EPD
(b) (4)	PR	Brimbelle	EPD	Primabella	EPD
Brasivol	EPD	Kristalose	EPD	Drisdol	EPD
Bravelle	EPD				
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Brisdelle	EPD				

Our analysis of the 17 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 17 names will not pose a risk for confusion as described in Appendices D through E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Reproductive and Urologic Products via e-mail on January 14, 2013. At that time we also requested additional information or concerns that could inform our review. The Division of Reproductive and Urologic Products did not state any additional concerns with the proposed proprietary name, Brisdelle.

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 Marcus Cato, OSE project manager, at 301-796-3903.

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3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Brisdelle, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your December 26, 2012 submission are altered, the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

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 Applicant 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/Applicant 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 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.

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

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 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. 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**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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 gather 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 posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

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

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

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

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 Applicant 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 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/Applicant. 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 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.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Brisdelle	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'B'	Pr, K, R, F, G, D, Ps, 13	P, V, D
1ower case 'b'	l, h, k, lo, le, t, lr, tr,li	p, v, d
lower case 'r'	S, n, e, v	None
lower case 'i'	e, l, j	Y
Lower case 's'	G, 5, g, n, a	x, z
Lower case 'd'	cl, ci, ol, a, el, v	b, t
lower case 'e'	a, i, l, o, u, p, c	Any vowel sound
lower case 'l'	b, e, s, A, P, i	None
Letter strings		
Letter string 'br'	Fr, tr, lr, bu, bv	Pr
Letter string 'ri'	U	
Letter string 'is'	U	Iz
Letter string 'el'	A, d, il, al, ei, cl, dc	Al, il
Letter string 'ell'	Eu	
Letter string 'le'	b, u	
Letter string 'lle'	ler	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Brisdelle Study (Conducted on 1/4/13)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Brisdelle 7.5 mg po hs	Brisdelle 1 orally every night #30
Outpatient Prescription: Brisdelle Sig: 1 po qhs Disp: #30	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

190 People Received Study
35 People Responded

Study Name: Brisdelle

Total	12	10	13	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
BREYSTIL	0	1	0	1
BRINDELLE	2	0	0	2
BRISDALE	0	1	0	1
BRISDELE	0	0	1	1
BRISDELEA	0	0	1	1
BRISDELEC	0	0	5	5
BRISDELEE	0	0	1	1
BRISDELER	0	0	1	1
BRISDELL	0	2	0	2
BRISDELLA	0	0	1	1
BRISDELLE	6	0	2	8
BRISDELLE 7.5 MG	1	0	0	1
BRISDILLE	1	0	0	1
BRISDOW	0	1	0	1
BRISDYL	0	1	0	1
BRISTEL	0	1	0	1
BRISTOW	0	2	0	2
BRIZDEL	0	1	0	1
BRUSDELEE	0	0	1	1
BURDELLE	1	0	0	1
BUSDELLE	1	0	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Brisdelle	Failure preventions
1.	Brisdelle	Paroxetine	Look and sound	Proposed proprietary name being evaluated in this review.
2.	Brimbelle	N/A	Look and sound	Name identified in the Natural Medicines database only. It is one of many different names used to reference bilberry leaves. No product characteristics could be found on Brimbelle in the common databases available. Additionally, there is no evidence of Brimbelle or Bilberry being prescribed in practice.
3.	Tridil	Nitroglycerin	Look	The pair has sufficient orthographic differences.
4.	Brasivol	Aluminum Oxide	Look	The pair has sufficient orthographic differences.
5.	Brickellia	N/A	Look	Name identified in Natural Medicines database only, with no products listed that contain this plant. It is also known as Hierba Dorada or Oregano de Monte. No other information regarding the product characteristics could be identified in the common databases available.
6.	(b) (4)	(b) (4)	Look	(b) (4)
7.	Brondelate	Guaifenesin and Oxtriphylline	Look	The pair has sufficient orthographic differences. Additionally, this product is no longer marketed and there are no generic equivalents available in the market.

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

No.	Proprietary Name	Active Ingredient	Similarity to Brisdelle	Failure preventions
8.	Primabella	N/A	Look	Name identified as a device and not a medication in Red Book online database. Further search of the Dogpile database provided the following information. A non-invasive prescription therapeutic FDA approved, Class II neuromodulation device worn on the wrist, for the treatment of nausea and vomiting due to pregnancy. There are no product characteristics (i.e., route of administration, dosage form, frequency of administration, strength, and dose). This medical device has to be ordered by the healthcare professionals by completing and faxing the referral form to a number. A patient care coordinator will then call the healthcare professional to confirm and process the order.

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.	**Proprietary name: Brisdelle (Paroxetine)** **Dosage form: Capsules** **Strength:7.5 mg** **Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime**	**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.	Brilinta (Ticagrelor) Tablets 90 mg Usual Dose: Initiate treatment with 2 tablets (180 mg) oral loading dose. Continue with 1 tablet (90 mg) twice daily.	Orthographic: Both names share the same beginning letter string 'Bri-', a similar position upstroke (fifth position 'd' vs. fourth position 'l'), and similar scripted ending letter strings ('-le' vs. '-ta'). Route of Administration: Oral Dosage Form: Solid oral Strength: Single strength Partial Overlap in the Frequency of Administration: Once Partial overlap in the Usual Dose: One (capsule vs. tablet)	Orthographic: The extra letter 's' in conjunction with the round part of the letter 'd' in Brisdelle provide a longer length between the upstrokes 'B' and 'd' in Brisdelle (vs. the length between the upstrokes 'B' and 'l' in Brilinta). Additionally, the sixth position upstroke 'l' in Brisdelle (vs. the letter 'n' in Brilinta) provides a different shape for this name and can help differentiate Brisdelle and Brilinta when scripted.

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
2.	Drisdol (Ergocalciferol) Capsules 1.25 mg (50,000 units Vitamin D) Usual Dose: Vitamin D resistant Rickets: 12,000 to 500,000 units daily. Hypoparathyroidism: 50,000 units to 200,000 units (or one to four) capsules daily concomitantly with calcium lactate 4 gram, six times per day.	Orthographic: Both names share similar scripted beginning letters ('B' vs. 'D'), the letter string '-risd-' in the same position of each name followed by similar scripted round vowels ('e' vs. 'o') and the upstroke 'l'. Route of Administration: Oral Dosage form: Capsules Strength: Single strength Partial Overlap in the Frequency of Administration: Once daily Overlap in the Usual Dose: One capsule	Orthographic: The extra ending letter string '-le' in Brisdelle provides a longer appearance for this name and can help differentiate Brisdelle and Drisdol when scripted.

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
3.	Brintellix*** (Vortioxetine) Tabelets 5 mg, 10 mg,15 mg, and 20 mg Usual Dose: The recommended starting dose is 10 mg orally once daily. Depending upon individual patient response at a 10 mg dose, the dose may be lowered to 5 mg or increased to a maximum of 20 mg once daily. (NDA (b) (4) and 204447; name found acceptable in OSE Review #'s 2012-1142 and 2012-2333, dated October 25, 2012. The Application is currently pending approval)	Orthographic: Both names share the beginning letter string 'Bri-' followed by similar scripted letters ('s' vs. 'n'), a fifth position upstroke ('d' vs. 't') followed by the letter string '-ell-' and similar scripted letters in the ninth position of each name ('e' vs. 'i'). Route of Administration: Oral Dosage form: Solid oral Partial Overlap in the Frequency of Administration: Once daily Partial Overlap in the Usual Dose: One (capsule vs. tablet)	Orthographic: The extra ending letter 'x' in Brintellix*** provides a longer length for this name and can help differentiate Brisdelle and Brintellix*** when scripted.

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

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
4.	Baraclude (Entecavir) Tablets 0.5 mg, 1 mg Solution, 005 mg/mL Usual Dose: 0.5 mg to 1 mg (or one tablet) orally once daily. Dose adjustments are required for patients with renal impairment.	Orthographic: Both names consist of nine letters, share the beginning letter 'B', similar position letter 'r' (second vs. third), similar scripted letter string and letter in the same position of each name ('d' vs. '-cl-') followed by similar scripted letters ('e' vs. 'u'), an eighth position upstroke ('l' vs. 'd'), and the ending letter 'e'. Route of Administration: Oral Overlap in the Dosage form: Solid oral Overlap in the Frequency of Administration: Once daily Partial Overlap in the Usual Dose: One (capsule vs. tablet)	Orthographic: The ending letter string '-ell-' in Brisdelle appears different than the letter string '-ud-' when scripted and can help differentiate Brisdelle and Baraclude when scripted. Strength: Single strength (7.5 mg) vs. multiple strengths (0.5 mg and 1 mg)

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
5.	Brevibloc (Esmolol Hydrochloride) Injection 2,500 mg/250 mL (10 mg/mL) 2,000 mg/100 mL (20 mg/mL) 100 mg/10 mL (10 mg/mL) 100 mg/5 mL (20 mg/mL) Usual Dose: An initial loading dose of 0.5 mg/kg (500 mcg/kg) infused over a minute duration followed by a maintenance infusion of 0.05 mg/kg/min (50 mcg/kg/min) for the next 4 minutes is recommended.	Orthographic: Both names consist of nine letters, share the beginning letter string 'Br-' followed by similar scripted letters ('i' vs. 'e'), similar scripted letter strings in similar positions of each name ('-del- vs. '-ibl-'), and similar scripted ending letters ('e' vs. 'c'). Possible Partial Overlap in the Frequency of Administration: Once	Orthographic: The eighth position upstroke 'l' in Brisdelle (vs. letter 'o' in Brevibloc) provides a different shape for this name and can help differentiate Brisdelle and Brevibloc when scripted. Strength: Single strength (7.5 mg) vs. multiple strengths (10 mg/mL and 20 mg/mL or 2,500 mg, 2,000 mg, and 100 mg)
6.	Bravelle (Urofollitrpin) Injection 75 units Usual Dose: 150 units to 450 units intramuscularly or subcutaneously per day. Maximum duration of treatment is no more than twelve days.	Orthographic: Both names share the beginning letter string 'Br-' and the ending letter string '-elle'. Strength: Single strength Partial Overlap in the Frequency of Administration: Once daily.	Orthographic: The letter string '-isd-' in brisdelle does not appear similar to the letter string '-av-' in Bravelle when scripted and can help differentiate Brisdelle and Bravelle when scripted. Route of Administration: Oral vs. intramuscular or subcutaneous Usual Dose: One tablet (or 7.5 mg) vs. 150 units to 450 units.

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
7.	Kristalose (Lactulose) Powder for Solution Single packets of 10 gram and 20 gram Usual Dose: 10 gram to 20 gram orally daily. Dose may be increased to 40 gram daily.	Orthographic: Both names share similar scripted beginning letters ('B' vs. 'K') followed by the letter string '-ris-', a fifth position upstroke ('d' vs. 't') followed by similar scripted letter strings ('-el-' vs. '-al-'), and the ending letter 'e'. Route of Administration: Oral Partial Overlap in the Frequency of Administration: Daily Possible Partial Overlap in the Usual Dose: One (capsule vs. pack)	Orthographic: The eighth position upstroke 'l' in Brisdelle (vs. the letter string '-os-') in Kristalose provides a different shape for this name and can help differentiate brisdelle and Kristalose when scripted. Strength: Single strength (7.5 mg) vs. 10 gram or 20 gram

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
8.	(b) (4)		

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

No.	Proprietary name: Brisdelle (Paroxetine) Dosage form: Capsules Strength:7.5 mg Usual Dose: One capsule (or 7.5 mg) orally once daily at bedtime	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
9.	Brevital Sodium (Methohexital Sodium) Injection, 500 mg, 2.5 gram Usual Dose: Dosage is highly individualized. Adults: for induction of anesthesia, Dose may range from 50 mg to 120 mg or more intravenously but averages about 70 mg. The usual dosage in adults ranges from 1 to 1.5 mg/kg. The induction dose usually provides anesthesia for 5 to 7 minutes. For maintenance, 20 mg to 40 mg (2 mL to 4 mL of a 1% solution) may be given every 4 to 7 minutes. Pediatrics: 6.6 mg to 10 mg/kg of the 5% concentration administered intramuscularly. For rectal administration, the usual dose is 25 mg/kg using the 1% solution.	Orthographic: Both names share the beginning letter string 'Br-' followed by similar scripted letter strings in the same position of each name ('-is-' vs. '-ev-'), similar position letter and letter string ('d' vs. '-it-') followed by similar scripted letter strings ('-el-' vs. '-al').	Orthographic: The extra ending letter string '-le' in Brisdelle provides a longer length for this name and can help differentiate Brisdelle and Brevital when scripted. Dose: One tablet (or 7.5 mg) vs. an individualized, weight based dosing regimen with no overlap with 7.5 mg.

Appendix F: Summary of OSE Review #2012-1376, dated November 27, 2012

2.2.3 Medication Error Data Selection of Cases

The proposed proprietary name (b) (4) if upon entering the marketplace, would be a dual proprietary name with the currently marketed product Pexeva (Paroxetine Mesylate), also from Noven Therapeutics LLC. DMEPA searched the AERS database for medication errors involving Prozac and Sarafem, because this dual proprietary name exists and is similar to Pexeva and (b) (4) specifically looking to see if patients were being prescribed both Prozac and Sarafem at the same time. Prozac and Sarafem are dual proprietary names for Fluoxetine Hydrochloride, and both owned by Eli Lily and Co. In addition, medication errors involving Pexeva (Paroxetine Mesylate) and Paxil (Paroxetine Hydrochloride) were also searched, specifically looking to see if patients were being prescribed both Pexeva and Paxil at the same time.

The July 23, 2012 search of the Adverse Event Reporting System (AERS) database used the following search terms:

- MedDRA High Level Group Term: "Medication Errors"
- MedDRA High Level Terms: "Product Label Issues," "Product Packaging Issues," and "Product Quality Issues NEC."
- Trade Names: "Prozac" and "Prozac Weekly"
- Verbatim Term: "Pro%"

The search retrieved 18 cases. These cases were then searched using the keyword "Prozac."

After individual review, all 18 cases were excluded for the following reasons:

- 17 cases did not mention Prozac
    - 8 cases of wrong drug (Sarafem confused with Serophene, Singulair, or Saphris or vice versa) including actually being dispensed or filled wrong, or error caught prior to being dispensed or filled.
    - 1 case of wrong strength (Sarafem 20 mg dispensed instead of 10 mg).
    - 1 case of improper dose (overdose), where the patient intentionally overdosed himself on Sarafem and Paxil.
    - 1 case of deteriorated drug, where the expiration date of unit dose packaged Sarafem was earlier than the store printed discard after date.
    - 3 cases of sound alike names (Sarafem versus Serophene).
    - 2 cases of adverse events while on Sarafem or generic Sarafem.
    - 1 case of a complaint about the package insert's maximum dose being misleading for the indication of Sarafem.

- 1 case mentioned Prozac and adverse events when switched to Sarafem but no medication errors. This was the same case found when searching keyword "Sarafem" in the 2,626 Prozac cases.

The August 10, 2012 search of the Adverse Event Reporting System (AERS) database used the following search terms:

- MedDRA High Level Group Term: "Medication Errors"
- MedDRA High Level Terms: "Product Label Issues," "Product Packaging Issues," and "Product Quality Issues NEC."
- Trade Name: "Pexeva"
- Verbatim Term: "Pex%"

The search retrieved 3 cases. These cases were then searched using the keyword "Paxil."

After individual review, all 3 cases were excluded for the following reasons:

- 3 cases did not mention Paxil
    - 1 case of improper dose (intentional overdose in a suicide attempt).
    - 1 duplicate case.
    - 1 case of dose omission (missed 10 days of Pexeva due to being between insurances).

2.2.4 FDA Name Simulation Studies

Twenty-five practitioners participated in DMEPA's prescription studies. The interpretations did overlap with or appear or sound similar to the currently marketed (b) (4) products. Eight people in the inpatient prescription study and seven people in the outpatient prescription study correctly interpreted the name (b) (4) No one correctly interpreted the name in the verbal prescription study with seven people interpreting the name as (b) (4) and one person interpreting the name as (b) (4) One person in the outpatient prescription study interpreted the name as (b) (4) even though the prescription was written as (b) (4) with no (b) (4) at the end of the name. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.6 Comments from Other Review Disciplines

In response to the OSE, June 21, 2012 e-mail, the Division of Reproductive and Urologic Products (DRUP) 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 of Similar Names

Although the Sponsor intends to use a dual proprietary name for the active ingredient Paroxetine, the Sponsor did not provide any rational for using a dual proprietary name in their submission for the proposed proprietary name, (b) (4)

DRUP and DPP were initially contacted when the Sponsor had submitted the first proposed proprietary name Mesafem***. At that time neither DRUP nor DPP expressed

safety concerns with the Sponsor's proposal to use dual proprietary names. We again contacted both the (b) (4) review team in DRUP, and the Pexeva review team in DPP for input on the Sponsor's proposal to use dual proprietary names upon this submission of the name (b) (4) The (b) (4) review team did not express any safety concerns with the Sponsor's proposal to use dual proprietary names. From the Pexeva review team, two concerns were brought up from a member of the team that were administrative (difficulty comparing two labels with label updates) and safety related (the potential of concomitant therapy if the patient was on both (b) (4) and Pexeva). However, after explaining that administrative perspectives are not considered for dual proprietary names and that we have no evidence of concomitant therapy with similar products (i.e. Sarafem and Prozac), DPP did not have concerns regarding the dual proprietary names.

Introducing a dual proprietary name is not without risk. There is the risk of concomitant therapy of Paroxetine if practitioners and patients fail to recognize that both Pexeva and (b) (4) contain Paroxetine. However, this possibility currently exists because Paxil (Paroxetine Hydrochloride) and generic equivalents are currently marketed. Three AERS searches were run looking to see if there were any reports of concomitant use of Serafem and Prozac (products that have a similar situation to (b) (4) and Pexeva), or concomitant use of Pexeva and Paxil. Our AERS search resulted in no relevant reports (see section 2.2.3). Thus, as with our previous findings when Mesafem was submitted, DMEPA finds the use of a dual proprietary name acceptable for the Sponsor's Paroxetine Mesylate product.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Reproductive and Urologic Products via e-mail on August 20, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Reproductive and Urologic Products (DRUP) on August 23, 2012, they stated no additional concerns with the proposed proprietary name, (b) (4)

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

/s/

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03/14/2013

ZACHARY A OLESZCZUK
03/14/2013

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