CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205003Orig1s000

PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date:	April 14, 2013
Reviewer(s):	Janine Stewart, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Lisa Khosla, PharmD, MHA Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	Prestalia (perindopril arginine and amlodipine besylate) tablets 3.5 mg/2.5 mg; 7 mg/5 mg; 14 mg/10 mg
Application Type/Number:	IND 108233, NDA 205003
Applicant/Sponsor:	Symplmed
OSE RCM #:	2013-16650, 2014-17141

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Prestalia, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

The Investigational New Drug (IND) 108233 application was initially held by XOMA (US) LLC. (b) (4) Ownership and sponsorship of IND 108233 was transferred to Symplmed on August 20, 2013. Symplmed submitted a request to review the proposed proprietary name, Prestalia, under IND 108233 on December 9, 2013. Symplmed subsequently submitted a request for proprietary name review of the name Prestalia under New Drug Application (NDA) 205003 on March 21, 2014.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 9, 2013 and March 21, 2014 proprietary name submissions.

- Active Ingredient: perindopril arginine/amlodipine besylate
- Indication of Use: For the treatment of hypertension, (b) (4) not adequately controlled on monotherapy with (b) (4)
- Route of Administration: Oral
- Dosage Form: Immediate- release tablet
- Strength: 3.5 mg/2.5 mg; 7 mg/5 mg; 14 mg/10 mg
- Dose and Frequency: Starting dose: 3.5 mg/2.5 mg po once daily, (b) (4) The maximum recommended dose is 14 mg/10 mg po once daily.
- How Supplied: (b) (4) ct bottles for all strengths. (b) (4)
- Storage: Controlled room temperature of (b) (4) 25°C (b) (4) 77°F) with excursions permitted between 15°C and 30°C (59°F and 86°F).
- Container and Closure Systems: 100 mL (b) (4) white, high density polyethylene (HDPE), wide mouth round bottles and capped (b) (4) an induction seal. Each bottle also contains a polyester pharmaceutical coil and a 1 gram silica gel desiccant canister.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The December 19, 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 did not indicate in their submission the derivation or an intended meaning of the proposed name, Prestalia. 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.

2.2.3 FDA Name Simulation Studies

Fifty-six practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. A trend we observed was four practitioners were unable to discern the 't' sound during the voice study of the name Prestalia and; therefore, omitted the letter 't' in their written interpretations of the name. Further, during the voice study, four participants misinterpreted the 'Pr' sound in the prefix of the name Prestalia and instead heard the prefix 'Per'. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, December 20, 2013 And April 2, 2014 e-mails, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 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, Prestalia. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Prestalia

identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation or the Drug Safety Institute (DSI) not identified by DMEPA and require further evaluation.

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

Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Pregabalin	external	Prostatonin	EPD	Prostin VR	EPD
Priscoline	EPD	Prostigmin	EPD	(b) (4)	EPD
Prostagen	EPD	Prostin E2	EPD		
Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Brisdelle	EPD	Kristalose	EPD	Prostaphlin	EPD
Crytselle	EPD	Prolia	EPD	Prostascint	external
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Prezista	external	Procardia	EPD	Restasis	EPD /external
Pristiq	external	Restall	EPD	Trelstar	EPD

Our analysis of the 20 names contained in Table 1 determined 20 names will not pose a risk for confusion as described in Appendices D through E.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on April 2, 2014. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Cardiovascular and Renal Products (DCRP) on April 7, 2014, they stated no additional concerns with the proposed proprietary name, Prestalia.

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 Karen Bengtson, OSE project manager, at 301-796-3338.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your December 9, 2013 and March 21, 2014 submissions are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

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

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

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

9. ***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.

10. ***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.

11. ***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.

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

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

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

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

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

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

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

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

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

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

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

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

18. 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.

19. Natural Standard (http://www.naturalstandard.com)

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

APPENDICES

Appendix A

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

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

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

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

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

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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.

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

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

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

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

Type of Similarity	**Considerations when Searching the Databases**		
	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 Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

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

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

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

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

Letters in Name, Prestalia	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'P'	F, B, R, D, T	B, C
Lower case 'p'	yn,, ys, g,j, l, q	b, c
Lower case 'r'	n, v, i	l
Lower case 'e'	a, i, l, o, r, u, p	Any Vowel
Lower case 's'	d, f, K, P, t, r, U,V,Y	z
Lower case 't'	d, t, l, x, s	d
Lower case 'a'	c, e, ei, el, ci, cl, d, n, o, u	Any vowel
Lower case 'l'	b,e, s,P, i	
Lower case 'i'	e, l, s	
Letter Strings		
Pr	R	Per
re	u	
ia	w	ar
li	b	
al	d	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Prestalia Study (Conducted on December 19, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Prestalia 7mg/5mg po once daily	Prestalia 3.5/2.5 Dispense number 30 Directions: Take one by mouth daily.
Outpatient Prescription: Prestalia 3.5/2.5 Sig: 1 PO daily Disp: #30	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Prestalia

As of Date 3/5/2014

199 People Received Study

56 People Responded

Study Name: Prestalia

Total	18	20	18	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CRISTALIZ	0	1	0	1

PERSTAHLIA	0	1	0	1
PERSTALIA	0	2	0	2
PERSTYLEA	0	1	0	1
PRASTALIA	0	1	0	1
PRESALIA	0	2	0	2
PRESARIA	0	1	0	1
PRESTALIA	14	7	1	22
PRESTALIA 3.5/2.5	1	0	0	1
PRESTALIC	3	0	0	3
PRESTALIN	0	0	1	1
PRETALAR	0	0	1	1
PRETHALIA	0	1	0	1
PRIRTALIA	0	0	1	1
PRISTALIA	0	2	13	15
PRISTALIO	0	0	1	1
PROSALIA	0	1	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 Prestalia	Failure preventions
1.	Brisdelle	paroxetine	Phonetic	The pair has sufficient phonetic differences.
2.	Crytselle		Phonetic	This name was identified in the POCA database. No additional information was found in any other commonly used databases. Additionally, the pair has sufficient phonetic differences.
3.	Kristalose	lactulose	Phonetic	The pair has sufficient phonetic differences.
4.	Priscoline	tolazoline hydrochoride	Orthographic	This name was identified in Micromedex database. No additional information was found in any other commonly used databases. Additionally, the pair has sufficient orthographic differences.
5.	Pristiq	desvenlafaxine succinate	Orthographic & Phonetic	The pair has sufficient orthographic and phonetic differences.
6.	Prostatonin	pygeum africanum/ urtica		The pair has sufficient orthographic differences.
7.	Prostascint	capromad pendetide	Phonetic	The pair has sufficient phonetic differences.
8.	Prostigmin	neostigmine bromide	Orthographic	The pair has sufficient orthographic differences.
9.	Prostin E2	dinoprostone	Orthographic	The pair has sufficient orthographic differences.
10.	Prostin vr	alprostadil	Orthographic	The pair has sufficient orthographic differences.
11.	[redacted] (b) (4)	carvedilol phosphate, lisinopril	Orthographic	[redacted] (b) (4) Additionally, the pair has sufficient orthographic differences.

No.	Proprietary Name	Active Ingredient	Similarity to Prestalia	Failure preventions
12.	Restall	hydroxyzine hydrochoride	Orthographic & Phonetic	The pair has sufficient orthographic and phonetic differences.

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

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Pregabalin** Strength: Oral Capsule: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg Oral Solution: 20 mg/ml Usual Dose: Diabetic peripheral neuropathy - Neuropathic pain: initial, 50 mg ORALLY three times a day (150 mg/day) and may be increased to MAX dose 100 mg ORALLY three times a day (300 mg/day) within 1 week based on efficacy and tolerability Fibromyalgia: initial, 75 mg ORALLY twice daily (150 mg/day), may increase to 150 mg twice daily (300 mg/day)	Orthographic: Both names begin with the letter string 'Pre' and have the same number of upstroke letters in similar positions. The ending letter string 'lin' in the name Pregabalin may look similar to the ending letter string 'lia' in the name Prestalia when scripted. Route of Administration: Both products are taken orally. Strength: There are partial numerical similarities of strength between Pregabalin 25 mg, 50 mg, and 100 mg capsules and Prestalia 3.5mg/**2.5mg**, 7 mg/ **5mg**, and 14mg/**10mg** tablets.	Orthographic: The name Pregabalin contains a down stroke letter 'g' while the name Prestalia does not contain a down stroke letter. In addition, the letter 'g' in pregabalin lengthens the infix prior to the first upstroke letter compared to the name Prestalia. These differences give the names a different shape when scripted. Strength: Pregabalin is a single ingredient product with one strength expression while Prestalia is a two-ingredient product Both products are available in multiple strengths and the strengths must be specified when prescribed Dose:

No.	Proposed name: Prestalia Dosage Form(s): oral tablet Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg Usual Dose: one tablet orally once daily	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
	within 1 week determined by tolerability and efficacy to a MAX of 225 mg twice daily (450 mg/day) Neuropathic pain - Spinal cord injury: initial, 75 mg ORALLY two times daily; may increase to 150 mg ORALLY two times daily within 1 week based on efficacy and tolerability; may further increase to 300 mg ORALLY 2 times daily for insufficient pain relief after 2 to 3 weeks of treatment Partial seizure; Adjunct: initial, no greater than 75 mg ORALLY two times daily OR 50 mg ORALLY three times daily (150 mg/day) and increased to a maximum dose of 600 mg/day in divided doses (either two or three times daily) based on response and tolerability Post herpetic neuralgia: initial, 75 mg ORALLY two times a day OR 50 mg ORALLY three times a day; may be increased to 300 mg/day within 1 week based on efficacy and tolerability Post herpetic neuralgia: maintenance, 75 to 150 mg ORALLY two times a day		There is no overlap or numerical similarity of dose between the two products.

No.	Proposed name: Prestalia Dosage Form(s): oral tablet Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg Usual Dose: one tablet orally once daily	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
	OR 50 to 100 mg ORALLY three times a day (150 to 300 mg/day) Post herpetic neuralgia: lack of effect, patients who do not experience sufficient pain relief following 2 to 4 weeks of treatment with 300 mg/day and are tolerating pregabalin, may increase dosage up to 300 mg two times a day, or 200 mg three times a day (600 mg/day)		

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Prostagen** (soybean) oral powder Usual Dose: CORONARY HEART DISEASE, PREVENTION, oral: 25 grams daily HOT FLUSH, oral: 50 to 150 milligrams of soy isoflavones daily HYPERLIPIDEMIA, oral: 25 grams daily to lower blood cholesterol levels MENOPAUSE, oral: 200 milligrams soy isoflavones daily OSTEOPOROSIS PREVENTION, oral: 40 to 80 milligrams soy isoflavones daily	Orthographic: The letter string 'Prosta' in the name Prostagen may look similar the letter string 'Presta' in the name Prestalia when scripted. The ending letter string 'en' in the name Prostagen can look like the ending letter string 'ia' in the name Prestalia when scripted. Frequency: Both products may be taken once daily. Route of Administration: Both products are taken orally. Dose: There are partial numerical similarities of dose between Prostagen 25 grams and 50 mg, and Prestalia 3.5mg/**2.5mg** and 7mg/**5mg**.	Orthographic: The name Prostagen contains a down stroke letter 'g' while the name Prestalia contains no down stroke letters which provides an orthographic difference when scripted.

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Prolia** (denosumab) injection Strength: 60 mg/ml Usual Dose: 60 MG administered as a single subcutaneous injection once every 6 months.	Phonetic: Both names begin with the 'Pr' sound and end with the 'lia' sound.	Phonetic: The name Prolia contains 3 syllables while the name Prestalia contains 4 syllables. Frequency of Administration: Prolia is administered once every 6 months while Prestalia is administered once daily. Strength: Prostagen is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Prestalia is available in multiple strengths while Prostagen is available as a single strength. The strengths of Prestalia must be specified when prescribed. There are no overlapping strengths. Dose: There is no overlap or numerical similarity of dose between the two products.

No.	Proposed name: Prestalia Dosage Form(s): oral tablet Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg Usual Dose: one tablet orally once daily	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.	**Prostaphlin** (oxacillin sodium) powder for injection Strength: 1 gm, 2 gm, 10 gm Usual Dose: **Infective endocarditis**: 12 g/day IV in 4 to 6 equally divided doses for 6 wks. WITH or WITHOUT gentamicin sulfate 3 mg/kg/day IV/IM in 2 or 3 equally divided doses for 3 to 5 days **Staphylococcal Infection** (mild to moderate): 250 to 500 mg IM or IV every 4 to 6 hr. (severe infections): 1 g IM or IV every 4 to 6 hr.	Phonetic: The first and second syllables sound similar in both names.	Phonetic: The name Prostaphlin contains 3 syllables while the name Prestalia contains 4 syllables. Additionally, the endfix 'lin' in Prostaphlin sounds different from the endfix 'lia' in Prestalia. Frequency of Administration: Prostaphlin is administered 2 to 6 times daily while Prestalia is administered once daily. Strength: Prostaphlin is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Both products are available in multiple strengths; therefore, the strengths must be specified when prescribed. There are no overlapping strengths. Dose: There is no overlap or numerical similarity of dose between the two products.

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Prezista** (darunavir) tablet, oral suspension Strength: 75 MG, 150 MG, 400 MG, 600 MG, 800 MG Suspension: 100mg/mL Usual Dose: Patients with no darunavir resistance associated substitutions- 800 mg (one 800 mg tablet or two 400 mg tablets) or 8 mL (oral suspension) once daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL (oral solution) once daily and with food Patients with at least one darunavir resistance associated substitutions- 600 mg (e.g. one 600 mg tablet) or 6 mL (oral suspension) twice daily with ritonavir 100 mg (one 100 mg tablet/capsule or 1.25 mL (oral solution) twice daily and with food	Orthographic: Both names begin with the letter string 'Pre'. Phonetic: The beginning sound 'Prez' in the name Prezista sounds similar to the beginning sound 'Pres" in the name Prestalia. Both names contain 3 syllables. Frequency: Both products may be taken once daily. Route of Administration: Both products are taken orally.	Orthographic: The name Prezista contains one cross stroke letter 't' while Prestalia has one cross stroke letter 't' and one upstroke letter 'l' providing orthographic differences when scripted. Phonetic: The name Prezista contains 3 syllables while Prestalia contains 4 syllables. The 'z' sound at the onset of the second syllable in the name Prezista sounds different from the 'st' sound at the onset of the second syllable in the name Prestalia. Additionally, the endfix 'ta' in Prezista sounds different from the endfix 'lia' in Prestalia. Strength: Prezista is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Both are available in multiple strengths; therefore, the strengths must be specified when prescribed. There are no overlapping strengths. Dose: There is no overlap or numerical similarity of dose between the two products.

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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**
6.	**Procardia** (nifedipine) capsule Strength: 10 mg Usual Dose: The starting dose is one 10 mg capsule, swallowed whole, 3 times/day. The usual effective dose range is 10–20 mg three times daily. Max daily dose – 180 mg	Orthographic: The beginning letter string 'Pro' in the name Procardia may look similar to the beginning letter string 'Pre' in the name Prestalia when scripted. The letter string 'al' can be scripted to look like the letter 'd'. Both names end in the letter string 'ia'. Phonetic: Both names contain 4 syllables. Both names begin with the 'Pr' sound and end with the 'ia' sound. Route of Administration: Both products are taken orally.	Orthographic: The name Procardia contains one upstroke letter 'd' while the name Pestalia has one cross stroke letter 't' and one upstroke letter 'l' providing orthographic differences when scripted. Phonetic: The 'c' sound at the onset of the second syllable in the name Procardia sounds different from the 'st' sound at the onset of the second syllable in the name Prestalia. The suffix 'dia' in the name Procardia sound different from the suffix 'lia' in the name Prestalia. Strength: Procardia is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Prestalia is available in multiple strengths while Procardia is available as a single strength. The strengths of Prestalia must be specified when prescribed.

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Restasis** (cyclosporine) Ophthalmic emulsion Strength: 0.05% Usual Dose: 2 applications per day	Orthographic: The 'Pr' in the name Prestalia can be scripted to look like the letter 'R'. Both names contain the letter string 'esta' in similar position. Phonetic: The beginning letters 'Rest' in the name Restasis sound similar to the letters' Prest' in the name Prestalia.	Orthographic: The suffix 'sis' in the name Restasis looks dissimilar to the suffix 'lia' in the name Prestalia. The name Prestalia contains one additional upstroke letter giving the name a different shape when scripted compared to the name Restasis. Phonetic: The name Restasis contains 3 syllables while the name Prestalia contains 4 syllables. The suffix 'sis' in the name Restasis sounds different from the suffix 'lia' in the name Prestalia. Strength: Restasis is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Prestalia is available in multiple strengths while Restasis is available as a single strength. The strengths of Prestalia must be specified when prescribed. There is no overlap of strengths. Dose: 2 applications or UAD (Restasis) vs. 1 tablet (Prestalia)

No.	**Proposed name: Prestalia** **Dosage Form(s): oral tablet** **Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg** **Usual Dose: one tablet orally once daily**	**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.	**Trelstar** (triptorelin pamoate) lyophilized powder for suspension Strength: 3.75 mg, 11.25 mg, 22.5 mg Usual Dose: 3.75 mg- 1 IM injection every 4 weeks 11.25 mg- 1 IM injection every 12 weeks 22.5 mg- 1 IM injection every 24 weeks	Orthographic: The 'Tre' in the name Trelstar can be scripted to look like the 'Pre' in the name Prestalia. Both names contain 2 upstroke letters giving the names orthographic similarities when scripted. Phonetic: The second syllable of both names, 'sta', sounds identical.	Orthographic: The name Prestalia has one additional letter 's' prior to the first upstroke letter which lengthens the prefix and gives the name a different shape when scripted compared to the name Trelstar. The suffix 'star' in the name Trelstar looks different from the suffix 'lia when scripted. Phonetic: The name Trelstar contain 2 syllables while the name Prestalia contains 4 syllables. Strength: Trelstar is a single ingredient product with one strength expression while Prestalia is a two-ingredient product. Both products are available in multiple strengths; therefore, the strengths must be specified when prescribed. There are no overlapping strengths. Frequency: Trelstar is given every 4, 12, or 24 weeks while Prestalia is given once daily. Dose: There is no overlap or numerical similarity of dose between the

No.	Proposed name: Prestalia Dosage Form(s): oral tablet Strength(s): 3.5 mg/2.5 mg, 7 mg/ 5 mg, 14 mg/ 10 mg Usual Dose: one tablet orally once daily	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
			two products.

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/s/

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