CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125387Orig1s000

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:	November 04, 2011
Reviewer(s):	Walter Fava, RPh, MSEd, Safety Evaluator W Fava 11-4-11 Division of Medication Error Prevention and Analysis
Team Leader	Zachary Oleszczuk, PharmD, Team Leader 11-4-11 Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Director C Holquist 11-4-11 Division of Medication Error Prevention and Analysis
Drug Name(s):	Eylea (Aflibercept) Injection 2 mg/0.05 mL
Application Type/Number:	BLA 125387
Applicant/sponsor:	Regeneron
OSE RCM #:	2011-3160

*** 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, Eylea is written in response to the anticipated approval of this BLA within 90 days from the date of this review. DMEPA found the proposed name, Eylea, acceptable in OSE Review # 2011-538 dated May 25, 2011.

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 or proposed since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2011-538 and 2010-1480. Since none of the proposed product characteristics considered in the previous FMEA were altered, we did not re-evaluate previous names of concern. (b) (4) packaging configurations will be marketed (the 2 mg/0.05 mL single-use vial), this does not impact our FMEA results. The searches of the databases yielded no new names, thought to look or sound similar to Eylea and represent a potential source of drug name confusion.

DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

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 October 31, 2011. OPDP re-eviewed the proposed name on September 22, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Eylea, did not find the name promotional or identify any vulnerabilities that would result in medication errors with the additional name noted in this review. Thus, DMEPA has no objection to the proprietary name, Eylea, for this product at this time.

DMEPA considers this a final review; however, if approval of the BLA is delayed beyond 90 days from the date of this review, the Division of Transplant and Ophthalmolgy 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 Karen Townsend, OSE Project Manager, at 301-796-5413.

4 REFERENCES

1. **OSE Reviews**

   Fava, W. OSE Review #2011-538 and 2010-1480: Proprietary Name Review for Eylea, May 25, 2011.

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/category/4782.html)*

   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.

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 Mitigation

Date:	May 25, 2011
Application Type/Number:	IND 012462 BLA 125387
Through:	Carlos M Mena-Grillasca, RPh, Team Leader Cmena 5/25/2011 Carol Holquist, RPh, Director Carol Holquist 5/25/2011 Division of Medication Error Prevention and Analysis (DMEPA)
From:	Walter Fava, RPh, MSEd., Safety Evaluator Walter Fava 5-25-2011 Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s)/ Strength:	Eylea (Aflibercept) Injection 2 mg/0.05 mL
Licensee:	Regeneron Pharmaceuticals, Inc.
OSE RCM #:	2010-1480 2011-538

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CONTENTS

EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis' evaluation for the proposed proprietary name Eylea for Aflibercept Injection. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Eylea, acceptable for this product. DMEPA will notify the Licensee of these findings via letter.

We consider this a final review of the proposed proprietary name, Eylea. However, if the action on this BLA is delayed 90 days beyond the date of this review, the proposed proprietary name, Eylea, must be re-reviewed. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this findings and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Regeneron Pharmaceuticals, Inc dated December 9, 2010 under IND (b) (4), and February 28, 2011 under BLA 125387 for a promotional and safety assessment of the proposed proprietary name, Eylea.

1.2 REGULATORY HISTORY

This product is a pending BLA with a PDUFA action date of August 20, 2011.

1.3 PRODUCT INFORMATION

Eylea (Aflibercept) injection is a recombinant fusion protein comprised of portions of human Vascular Endothelial Growth Factor (VEGF) receptor 1 and 2 extracellular domains fused to the Fc portion of human IgGI for intravitreal administration by a qualified physician experienced in the administering of intravitreal injections in the treatment of Neovascular (wet) Age-Related Macular Degeneration (AMD) (b) (4) The product will be available in (b) (4) It will also be available in single-use glass vials containing 0.05 mL of a 40 mg/mL solution. The recommended dose is 2 mg (0.05 mL) administered by intravitreal injection monthly for the first three months, followed by 2 mg once every two months. . The product is to be stored refrigerated at 2°C to 8°C (36°F to 46°F), protected from light. Vials will be supplied with a 5 micron 19 gauge, 1½ inch needle for withdrawal of the vial contents (b) (4) and a 30 gauge, ½ inch needle with a 1 mL (b) (4) syringe for administration. (b) (4) (b) (4)

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to Eylea, the DMEPA safety evaluators also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (five letters), upstrokes (two, capital letter 'E' and lower case 'l'), down strokes (one, lower case 'y'), cross strokes (none), and dotted (none). Additionally, several letters in Eylea may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA safety evaluator also considers these alternate appearances when identifying drug names that may look similar to Eylea.

When searching to identify potential names that may sound similar to Eylea, the safety evaluators search for names with similar number of syllables (three), stresses (EY-le-a, ey-LE-a, and ey-le-A) and placement of vowel and consonant sounds (See Appendix B). The Licensee's intended pronunciation (I-lee-ah) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 PRESCRIPTION ANALYSIS STUDIES

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

3 RESULTS

The names identified from DMEPA's methods as potential sources for name confusion with Eylea are listed below.

3.1 DATA BASE AND INFORMATION SOURCES

The searches yielded a total of 25 names as having some similarity to the name Eylea.

Twenty-three of the names were thought to look like Eylea. These include: Iplex, Alera, Alora, (b) (4) Epitol, Erytab, Zylet, Extina, Exelon, Egrifta, Epiduo, Ery, Eryc, Evista, Exna, Cylex, Cydec, Ceftin, Cytra-2, Cytra, Cycrin, Alfexa, and Cyotic. One of the names, Pylera, was thought to sound like Eylea. The remaining name, Ella, was thought to look and sound similar to Eylea.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 23, 2011.

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

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

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 PRESCRIPTION ANALYSIS STUDIES

A total of 34 practitioners responded to the study with one response from the inpatient order overlapping with the existing name Zyban, and three responses from the outpatient prescription overlapping with the existing name Zyrtec. None of the participants interpreted the name correctly as "Eylea". We note the poor quality of the writing samples for the inpatient order and outpatient prescription. Nevertheless, both drug names, Zyban and Zyrtec, will be added to the FMEA analysis. In the verbal studies, three of the responses were correct, while the remaining responses were misspelled phonetic variations of the proposed name, Eylea. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF TRANSPLANT AND OPHTHALMOLOGY PRODUCTS (DTOP)

3.4.1 Initial Phase of Review

In response to the OSE December 22, 2011 e-mail, the Division of Transplant and Ophthalmology Products provided no concerns with the proposed proprietary name, Eylea.

3.4.2 Midpoint of Review

DMEPA notified the Division of Transplant and Ophthalmology Products via e-mail on May 13, 2011 that we found the proposed name, Eylea, acceptable. Per e-mail correspondence on May 19, 2011, they indicated that they had no additional comments regarding our evaluation of the proposed proprietary name, Eylea.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in two additional names, Cytra-3, Cytra-K, which were thought to look or sound similar to Eylea.

Thus, we evaluated a total of 29 names: 25 names identified in section 3.1 above, 2 names identified in the prescription analysis studies, and 2 names identified by the primary safety evaluator.

4 DISCUSSION

This proposed name, Eylea, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Transplant and Ophthalmolgy Products (DTOP) concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

DMEPA evaluated 29 names for their potential similarity to the proposed name, Eylea. No other aspects of the name were considered to pose a potential for confusion.

Two names were determined to not appear in usual clinical practice for the reasons described in Appendix D and thus eliminated from further evaluation.

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the 27 remaining names and lead to medication errors. This analysis determined that the name similarity between Eylea and all of these 27 identified names was unlikely to result in medication error for the reasons presented in Appendices E and F.

5 CONCLUSIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Eylea, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Eylea, for this product at this time. DMEPA will notify the Licensee of this determination via letter.

We consider this a final review of the proposed proprietary name, Eylea. However, if the action on this BLA is delayed 90 days beyond the date of this review, the proposed proprietary name, Eylea, must be re-reviewed.

If you have further questions or need clarifications, please contact Karen Townsend, project manager, at 301-796-5413.

5.1 COMMENTS TO THE LICENSEE

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

The proposed proprietary name, Eylea, will be re-reviewed 90 days prior to the approval of the BLA. If we find the name unacceptable following the re-review, we will notify you.

If any of the proposed product characteristics as stated in your February 28, 2011 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

DARRTS is a government database used to organize Licensee and Licensee 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. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

12. Access Med (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.

13. 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.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal

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

CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

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

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

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

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

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally,

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

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

other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Licensee's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Licensee has little control over how the name will be spoken in clinical practice.

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in 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 the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial

phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product 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 characteristics listed in Section one. 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?"***

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

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

name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Licensee select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Licensee 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 Licensee. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a

preventable source of medication error that, in many instances, the Agency and/or Licensee 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. Licensees have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Licensee 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 Licensees' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Licensee select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Licensee 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.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Eylea	Scripted may appear as	Spoken may be interpreted as
Capital 'E'	'I', 'l', 'z', 'F', 'Z'	any vowel
lower case 'y'	'g', 'j', 'p', or 'z'	'i' or 'e'
lower case 'l'	'i'	--
lower case 'e'	any vowel	any vowel
lower case 'a'	c, 'ce,' 'ci,' e, o, or u	any vowel

Appendix C: Prescription study samples and results

Figure 1. Eylea Study (conducted on 12/22/2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Medication Order : Eylea 2mg Intravitreal #1	Eylea 2 mg Bring to clinic #1
Outpatient prescription: Eylea Bring to Clinic #1 / Vial	

FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Zylera	Zylix	Ilea
Zyban	Zyfec	Imea
Zylan	Zyrtec	Illya
Zylflo	Zylec	Ilea
Eylon	Zyrtec	Ilea
Zylan	Zylea	Ilea
	Zyrtec	Alya
	Zipec	Elia
	Zylec	Ilea
	Zylec	Ilea
	Zylec	Ilea
	Zytec	
	Zylec	
	Zylec	
	Zylec	
	Zylec	
	Ziflex	

Appendix D: Proprietary names not used in usual clinical practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to	Failure preventions
Exna	benzthiazide	Look	Discontinued product with no commercially available generic therapeutic equivalent products
Cylex	benzocaine	Look	Discontinued product over-the-counter lozenge

Appendix E: Risk of name confusion minimized by preventions listed. (Potential contributing causes highlighted by *italics*)

Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**	**Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.**
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Iplex (mecasermin rinafabate) *Orthographic similarities: The beginning letter, 'E' in Eylea may appear similar to the beginning letter, 'I' in Iplex when scripted. Both names also contain a downstroke and an upstroke letter in the second and third positions. Additionally, they both contain the letters, 'le' in similar positions in the names.*	Look	36 mg/0.6 mL for injection	Children > 3 years inject 2 mg/kg subcutaneously daily	**Orthographic differences:** The ending letter, 'a' in Elyea looks different from the ending letter, 'x' in Iplex when scripted. **Frequency of Administration:** Monthly for 3 months then once every 2 months vs daily **Route of Adminstration:** Intravitreal vs subcutaneous

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Alera (hydroquinone) *Orthographic similarities:* *Both names contain five letters and have the overlapping letters, 'e', 'l', and 'a'. The beginning letter, 'E' in Eylea may look like the beginning letter, 'A' in Alera and both names contain two upstroke letters.*	Look	4% topical emulsion	Apply to affected area(s) twice a day	**Orthographic differences:** Eylea contains the downstroke letter, 'y' which Alera does not have and may help differentiate the names when scripted. **Dosage Form:** Injection vs topical emulsion **Route of Administration:** Intravitreal vs topical **Frequency of Adminstration:** Monthly for 3 months followed by once every 2 months vs twice a day **Units of Measure:** mg vs %

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Alora (Estradiol Acetate) *Orthographic similarities:* *Both names contain five letters and have similar length when scripted. The beginning letter, 'E' in Eylea may look similar to the begining letter, 'A' in Alora. Both names end in the letter 'a'.*	Look	0.025 mg/24 hr, 0.05 mg/24 hr, 0.075 mg/24 hr, 0.1 mg/24 hr transdermal patch	Apply one patch topically once a day.	**Orthographic differences:** Eylea contains the downstroke letter, 'y' which Alora does not have and may help differentiate the names when scripted. **Strength:** Single (2 mg/0.05 mL) vs Multiple (0.025 mg/24 hr; 0.05 mg/24 hr; 0.075 mg/24 hr; 0.1 mg/24 hr) **Dosage Form:** Injection vs transdermal patch **Route of Administration:** Intravitreal vs topical **Frequency of Adminstration:** Monthly for 3 months followed by once every 2 months vs once a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	

(b) (4)

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Product name with potential for confusion	Similarity to Proposed Proprietary ~~Name~~	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated ~~product characteristics as~~ well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Epitol (carbamazepine) *Orthographic similarities: Both names begin with the letter, 'E', have a downstroke second letter, and contain the letter, 'l'.*	Look	200 mg tablet	Generalized tonic-clonic seizures and simple or complex-partial seizures: 200 mg by mouth twice a day Neuropathic pain: Initial dose of 100 mg by mouth twice a day titrate up to a maintenance dose of 600 mg to 800 mg in divided doses daily Postherpetic neuralgia: 100 mg to 300 mg by mouth three times a day Trigeminal neuralgia: Initial dose 100 mg by mouth twice a day titrate in 100 mg increments every 12 hours until symptoms are relieved up to a maximum daily dose of 1200 mg per day Bipolar Disorder: Initial dose of 200 mg by mouth daily titrate up to a maintenance dosage range of 600 mg to 1600 mg daily in divided doses Behavioral disturbances related to dementia: 100 mg by mouth twice a day titrate up to 250 mg to 300 mg per day in divided doses Persistent singultus: 200 mg by mouth three times a day	**Orthographic differences:** Eylea contains two upstroke letters, 'E' and 'l' compared to three upstroke letters, 'E', 't', and 'l' in Epitol. The ending upstroke letter, 'l' in Epitol may help differentiate the names when scripted. **Dosage Form:** Injection vs tablet **Route of Administration:** Intravitreal vs Oral **Frequency of Administration:** Monthly for 3 months followed by once every 2 months vs twice a day or three times a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Zylet (loteprednol and tobramycin) *Orthographic similarities: Both names contain five letters and contain the letters, 'y', 'l', and 'e'.*	Look	0.5% and 0.3% Ophthalmic suspension	Apply 1 to 2 drops into conjunctival sac of the affected eye(s) every 4 to 6 hours.	**Orthographic differences:** Eylea contains two upstroke letters, 'E' and 'l' compared to three upstroke letters, 'Z', 'l', and 't' in Zylet. Also, the upstroke, cross-stroke letter, 't' at the end of Zylet may help differentiate it from Eylea when scripted. **Dosage Form:** Injection vs ophthalmic suspension **Frequency of Administration:** Once monthly for 3 months followed by once every 2 months vs every 4 to 6 hours **Setting of Use:** Clinic or hospital vs home use for self administration

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Extina (ketoconazole) *Orthographic similarities: Both names begin with the letter, 'E' and end in the letter, 'a'. In addition, the second letter, 'y' in Eylea may look similar to the second letter, 'x' in Extina when scripted.*	Look	2% foam	Apply to affected areas twice a day for 4 weeks.	**Orthographic differences:** Eylea contains a downstroke letter, 'y' which Extina does not have and Extina contains the cross-stroke letter, 't' which Eylea does not have. These difference may help differentiate the names when scripted. **Dosage Form:** Injection vs foam **Route of Administration:** Intravitreal injection vs topical **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs twice a day for 4 weeks.

Product name with potential for confusion	Similarity to Proposed Proprietary ~~Name~~	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated ~~product characteristics as~~ well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Exelon (rivastigmine) *Orthographic similarities: Both names begin with the letter, 'E' and contain the letters, 'e' and 'l'.*	Look	4.6 mh/24 hr, 9.5 mg/24 hr, transdermal patch; 1.5 mg, 3 mg, **4.5 mg, and** 6 mg capsule	Capsule: Initial: 1.5 mg by mouth twice a day with food Maintenance: 3 mg to 12 mg daily in divided doses Patch: Apply one patch every 24 hours	**Orthographic differences:** Eylea has a downstroke letter, 'y' which Exelon does not have and the ending letters, 'ea' in Eylea appear different from the corresponding ending letters, 'on' in Exelon when scripted. These differences may help to distinguish this name pair when scripted. **Strength:** Single (2 mg/0.05 mL) vs Multiple (4.6 mg/24 hr; 9.5 mg/24 hr; 1.5 mg; 3 mg; 4.5 mg; 6 mg) **Dosage Form:** Injection vs topical patch and capsule **Route of Administration:** Intravitreal vs oral and topical **Frequency of Administration:** Once monthly for 3 months followed by once monthly every 2 months vs twice a day (capsule) or every 24 hours (patch)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Egrifta (tesamorelin) *Orthographic similarities: Both names begin with the letter, 'E' and end in the letter 'a'. In addition, the second letter of both names is a downstroke letter.*	Look	1 mg powder for injection	Inject 2 mg subcutaneously once a day.	**Orthographic differences:** Eylea contains two upstroke letters, 'E' and 'l' compared to three upstroke letters, 'E', 'f', and't', in Egrifta. **Route of Administration:** Intravitreal vs subcutaneous **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day
Epiduo (adapalene and benzoyl peroxide) *Orthographic similarities: Both names begin with the letter, 'E' and have a downstroke second letter. The ending letter, 'a' in Elyea may look smilar to the ending letter, 'o' in Epiduo.*	Look	1% and 2.5% topical gel	Apply a pea size amount to each area of the face after washing.	**Orthographic differences:** The letter string, 'yle' in Eylea looks different from the corresponding letter string, 'pid' in Epiduo, when scripted. **Dosage Form:** Injection vs topical gel **Route of Administration:** Intravitreal vs topical **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Ery-Tab (erythromycin) *Orthographic similarities: Both names begin with the letter, 'E' and contain the letter, 'y'.* Eryc (erythromycin estolate) *Orthographic similarities: Both names begin with the letter, 'E' and contain the letter, 'y'.* Ery (erythromycin)	Look	250 mg, 333 mg, and 500 mg delayed release tablets 250 mg capsule 125 mg/5 mL and 250 mg/5 mL suspension 2% pads	Acne vulgaris: 250 mg by mouth four times a day Haemophilus ducreyi: 500 mg by mouth four times a day for 7 days Severe Upper Respiratory Tract Infections or lower respiratory tract infections: 250 mg to 500 mg by mouth every 6 hours Chlamydia trachomatis: 50 mg/kg in four divided doses for 14 days Mycoplasma pneumonia: 250 mg to 500 mg by mouth three times a day Legionnaire's disease: 500 mg to 1000 mg by mouth every 6 hours for 21 days Group A beta-hemolytic streptococcal pharyngitis: 250 mg to 500 mg by mouth every 6 hours for 10 days Rheumatic fever: 250 mg by mouth twice a day Listeriosis: 250 mg to 500 mg by mouth every 6 hours	**Strength:** Single (2 mg/0.5 mL) vs multiple (250 mg, 333 mg, 500 mg, 125 mg/5 mL, 250 mg/5 mL, 2%) **Dosage Form:** Injection vs tablet, capsule, suspension, or pad **Route of Administration:** Intravitreal vs oral and topical **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs three times a day or every 6 hours (depending on the indication)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Evista *Orthographic similarities: Both names begin with the letter, 'E' and end in the letter, 'a'.*	Look	60 mg tablet	Osteoporosis prophylaxis: 60 mg by mouth once a day Uterine Leiomyomata in postmenopausal women: 60 mg by mouth daily in 28 day cycles Invasive breast cancer prophylaxis in postmenopausal women with osteoporosis or in postmenopausal women who are at high risk for developing the disease: 60 mg by mouth once a day	**Orthographic differences:** Eylea has a downstroke letter, 'y' compared to no downstroke letters in Evista. Additionally, Evista has a cross-stroke letter, 't', which Eylea does not contain. These orthographic differences may help distinguish this name pair when scripted. **Dosage Form:** Injection vs tablet **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Cydec (Carbinoxamine Maleate, Pseudoephedrine Hydrochloride) *Orthographic similarities: Both names contain five letters, appear similar in length and shape when scripted. Both names have the downstroke letter, 'y' in the second position followed by an upstroke third letter ('l' vs 't').*	Look	2 mg/25 mg/mL drops	Infants: 9-12 months: Two drops by mouth twice a day 6-9 months: One drop by mouth three times a day 3-6 months: One drop by mouth twice a day 1-3 months: One drop by mouth daily	**Dosage Form:** Injection vs oral drops **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day to every 8 hours depending on the age and weight of the child

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Ceftin *Orthographic similarities: The beginning letter, 'E' in Eylea may look similar to the beginning letter, 'C' in Ceftin.*	Look	125 mg, 250 mg, and 500 mg tablet 125 mg/5 mL and 250 mg/5 mL oral suspension	250 mg to 500 mg by mouth every 12 hours	**Orthographic differences:** Eylea contains two upstroke letters, 'E' and 'l' compared to three upstroke letters, 'C', 'f', and 't' in Ceftin. The ending portion, 'lea' in Eylea look different from the ending portion, 'tin' in Ceftin. **Strength:** Single (2 mg/0.05 mL) vs Multiple (125 mg, 250 mg, 500 mg, 125 mg/5 mL and 250 mg/5 mL) **Dosage Form:** Injection vs tablet and oral suspension **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs every 12 hours

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Cytra Cytra-2 (Sodium Citrate/Citric Acid) Cytra-3 (Tricitrates) Cyrtra-K (Potassium Citrate/Citric Acid) *Orthographic similarities: Both names contain five letters, making them appear similar in length and both have the overlapping letters, 'y' and 'a' in similar positions. The beginning letter, 'E' in Eylea may look similar to the beginning letter, 'C' in Cytra-2 when scripted.*	Look	NA	Dilute 3 to 6 teaspoonsful with water four times a day with meals and at bedtime	**Orthographic differences:** Eylea does not contain suffixes which are found in the Cytra product line and may help differentiate the names when scripted. **Dosage Form:** Injection vs oral solution or oral syrup **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs four times a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Cycrin (Medroxyproges - terone Acetate) *Orthographic similarities: Both names contain the downstroke letter, 'y' in the second position and the beginning letter, 'E' in Eylea may look similar to the beginning letter, 'C' in Cycrin when scripted.*	Look	2.5 mg tablets	One tablet by mouth once a day	**Orthographic differences:** Eylea has two upstroke letters, 'E', and 'l', compared to one upstroke letter, 'C' in Cycrin. The ending portion, 'lea' in Eylea looks different from the ending letters, 'crin' in Cycrin. **Dosage Form:** Injection vs tablet **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day

Product name with potential for confusion	Similarity to Proposed Proprietary ~~Name~~	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated ~~product characteristics~~ as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Aflexa (N-Acetyl-D-glucosamine) *Orthographic similarities:* *Both names contain the upstroke letter, 'l' and end in the letter, 'a'. The beginning letter, 'E' in Eylea may look similar to the beginning letter, 'A' in Alfexa. Both names also contain the lowercase letter, 'e' in similar positions.*	Look	500 mg Capsule	500 mg by mouth three times a day	**Orthographic differences:** Eylea contains two upstroke letters, 'E' and 'l', compared to three upstroke letters, 'A', 'f', and 'l' in Aflexa. Eylea also contains a downstroke letter, 'y' which Aflexa does not have. **Dosage Form:** Injection vs Capsule **Route of Administration:** Intravitreal vs Oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs three times a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Cyotic (Chloroxylenol, Hydrocortisone and pramoxine) *Orthographic similarities:* *Both names contain the downstroke letter, 'y' in the second position and the beginning letter, 'E' in Eylea may look similar to the beginning letter, 'C' in Cyotic when scripted.*	Look	0.1%; 1%; 1% Otic solution	Apply 5 drops into affected ear(s) three to four times daily.	**Orthographic differences:** Cyotic has an upstroke cross-stroke letter, 't' which Eylea does not have. **Dosage Form:** Injection vs Otic solution **Route of Administration:** Intravitreal vs Otic **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs three to four times a day

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Ella (Ulipristal Acetate) *<u>Orthographic similarities:</u> Both names begin with the letter, 'E', end in the letter, 'a', and have the overlapping letter, 'l' in the third position of both names.* *<u>Phonetic similarities:</u> Both names have similar sounding beginning syllables, 'Ey' vs 'El' and end in the same sound, 'a'.*	Look and Sound	30 mg tablets	Take one tablet by mouth within 72 hours after unprotected intercourse	**<u>Orthographic differences:</u>** Eylea has a downstroke letter, 'y' which Ella does not have. Eylea has two upstroke letters, 'E' and 'l' compared to three upstroke letter, 'E', 'l', and 'l', in Ella. **<u>Dosage Form:</u>** Injection vs tablet **<u>Route of Administration:</u>** Intravitreal vs oral **<u>Frequency of Administration:</u>** Once a month for 3 months followed by once every 2 months vs one time within 72 hours after unprotected intercourse.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Eylea (Aflibercept HCl)		2 mg/0.05 mL	2 mg by intravitreal injection once every month for 3 months, followed by 2 mg every 2 months.	
Pylera (Bismuth Subcitrate Potassium, Metronidazole, and Tetracycline Hydro-chloride) *Phonetic similarities: Both names contain three syllables with common, 'yl' and 'a' sounds in similar positions.*	Sound	140 mg; 125 mg; 125 mg capsules	Take three capsules by mouth four times a day with omeprazole following meals and at bedtime.	**Phonetic difference:** The beginning letter, 'P' in Pylera is distinctive from the beginning letter, 'E' in Eylea and the sound of the letter, 'r' in Pylera when spoken may also help to distinguish this name pair. **Dosage Form:** Injection vs capsule **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs four times a day

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

Proposed name:	**Strength:**	**Usual dose:**
Eylea **(Aflibercept HCl)**	**2 mg/0.05 mL**	**Inject 2 mg (0.05 mL) intravitreally once a month for 3 months followed by 2 mg intravitreal injections once every 2 months.**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Zyrtec (Cetirizine Hydrochloride) 5 mg, 10 mg tablets 1mg/mL syrup Usual dose: One tablet by mouth daily	Orthographic similarity: Both names have a downstroke letter, 'y' in the second position and have similar shapes and lengths when scripted. The beginning letter, 'E' in Eylea, may look similar to the beginning letter, 'Z' in Zyrtec when scripted.	Rationale Despite orthographic similarities between the names, the different product characteristics between these names may help prevent medication errors from any name confusion. Practitioners who incorrectly interpret the name for either product would not be able to fill an order or administer the wrong product based on the following differences between the products: **Strength:** Single (2 mg/0.05 mL) vs Multiple (5 mg, 10 mg) **Dosage Form:** Injection vs tablet **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs once a day.
Zyban (Bupropion Hydrochloride) 150 mg tablets Usual dose: One tablet by mouth twice a day	Orthographic similarity: Both names have a downstroke letter, 'y' in the second position and have similar shapes and lengths when scripted. The beginning letter, 'E' in Eylea, may look similar to the beginning letter, 'Z' in Zyban when scripted.	Rationale Despite orthographic similarities between the names, the different product characteristics between these names may help prevent medication errors from any name confusion. Practitioners who incorrectly interpret the name for either product would not be able to fill an order or administer the wrong product based on the following differences between the products: **Dosage Form:** Injection vs tablet **Route of Administration:** Intravitreal vs oral **Frequency of Administration:** Once a month for 3 months followed by once every 2 months vs twice a day.