CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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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:	November 28, 2011
Reviewer(s):	Richard A Abate, RPh, MS, Safety Evaluator Division of Medication Prevention and Analysis
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Division Director	Carol Holquist, RPh, Director Division of Medication Prevention and Analysis
Drug Name(s) and Strengths:	Erivedge (Vismodegib) Capsules, 150 mg
Application Type/Number:	IND 074573 NDA 203388
Applicant:	Genentech
OSE RCM #:	2011-2668 2011-3483

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

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Erivedge, 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 Applicant, Genentech, submitted a Request for Proprietary Name Review to the active IND application (074573) on August 2, 2011 after negotiating with DMEPA the timing as this product would likely be a priority review once submitted as an NDA. Additionally, the Applicant submitted a Request for Proprietary Name Review to the NDA 203388 on September 8, 2011 with the NDA. The NDA was granted Priority Review Designation on November 4, 2011.

1.2 PRODUCT INFORMATION

The following product information is provided in the August 2, 2011 proprietary name submission and draft package insert included with the NDA submission on September 8, 2011.

- Established Name: Vismodegib
- Indication of Use: The treatment of adult patients with advanced basal cell carcinoma for whom surgery is inappropriate
- Route of administration: Oral
- Dosage form: 150 mg capsule
- Dose: One capsule (150 mg) by mouth once daily.
- How Supplied: Bottles containing 28 capsules. Each bottle will be packaged in a carton.
- Storage: The product is stored at 68º F to 77º F (20º C to 25º C) with excursions permitted to 59º F to 86º F (15º C to 30º C).
- Container and Closure systems: A single 50 mL square white HDPE bottle with child resistant screw cap (b) (4)
- Intended pronunciation: EH-rih-vedge

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Oncology Products 2 (DOP2) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following sections are considered in the overall safety evaluation of the proposed name, Erivedge.

2.2.1 United States Adopted Names (USAN) SEARCH

On October 26, 2011, the United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

This proprietary name is compromised 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

Forty-three practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Of note, all respondents to the written samples (inpatient and outpatient) interpreted the name correctly as "Erivedge." The verbal responses were all phonetic variations on the name. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplies

In response to the OSE August 11, 2011 e-mail, the Division of Oncology Products 2 (DOP2) noted no concerns relating to the proposed name at the initial phase of the name 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 Erivedge. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Erivedge. These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), or other review disciplines. Table 1 also includes the names not previously identified by DMEPA but identified by (b) (4) a third party vendor, who completed an external name assessment for the proposed proprietary name for the Applicant.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and the third party vendor)

Look Similar		Sound Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Cervidil	FDA	Atrovent	FDA	Amerge	(b) (4)
Econazole	FDA	Eryped	FDA	Aricept	FDA (b) (4)
Eribulin	FDA	Feratab	FDA		
Ertaczo	FDA	Serevent	FDA		
Erycette	FDA	Veregen	FDA		
Estinyl	FDA	Aerobid	(b) (4)		
Evaclon	FDA	Erythromycin			
Exalgo	FDA	Aranesp			
Excedrin	FDA				
Erbitux	(b) (4)				
Eridium					
Evista					
Exforge					
Erwinaze	FDA				

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

2.2.6 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated these midpoint review findings to the Division of Oncology Products 2 (DOP2) via e-mail on November 3, 2011. At that time we requested DOP2 provide any information or concerns that could inform our review. Per e-mail correspondence from the DOP2 on November 9, 2011, they stated no additional concerns with the proposed proprietary name, Erivedge.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Erivedge, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your September 8, 2011 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review. Additionally, this proprietary name must be re-evaluated 90 days prior to the approval of the application. The conclusions upon re-review are subject to change.

4 REFERENCES

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

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

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

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

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

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

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. ***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 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.

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 promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by DDMAC. DDMAC 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. DDMAC 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 product characteristics considered for this review appears in Appendix B1 of this review.

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).

Table 2. 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*
	Similar spelling	Identical prefix	• Names may appear similar

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

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	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 Division of Drug Marketing, Advertising, and Communications (DDMAC). 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 DDMAC'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 characteristics listed in Appendix B1 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***

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

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. 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 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.

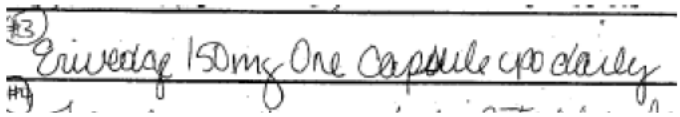
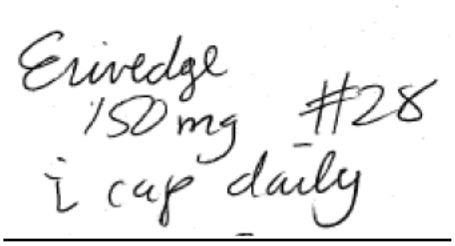
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors 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 C: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Erivedge	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'E'	C or F	any vowel
lower case 'e'	c, i, or l	any vowel
lower case 'r'	n, s, t, or v	'w'
lower case 'i' In combination 'iv'	c, e, or l w	any vowel
lower case 'v'	n, r, or u	'f'
lower case 'd'	'cl,' 'el,' or 'ol'	't'
lower case 'g'	j, q, s, y, or z	'j'

Appendix D: Prescription Simulation Samples and Results

Figure 1. Erivedge Study (Conducted on August 18, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  	Erivedge 150 mg The directions for use are to take one capsule by mouth daily. Dispense quantity number 28.
Outpatient Prescription:  	

FDA Prescription Simulation Responses.

INPATIENT	STRENGTH	VOICE	STRENGTH	OUTPATIENT	STRENGTH
ERIVEDGE	150 mg	ARAVEG	150 mg	ERIVEDGE	150 mg
ERIVEDGE	150 mg	ARAVEG	150 mg	ERIVEDGE	150mg
ERIVEDGE	150mg	ARAVENGE	150 mg	ERIVEDGE	150 mg
ERIVEDGE	150mg	AREVEG	150 mg	ERIVEDGE	150 mg
ERIVEDGE	150mg	ARIVAG	150 mg	ERIVEDGE	150mg
ERIVEDGE	150 mg	ARIVAGE		ERIVEDGE	150mg
ERIVEDGE	150mg	ARIVEG	150 mg	ERIVEDGE	150 mg
ERIVEDGE	150mg	ARIVEG	150mg	ERIVEDGE	
ERIVEDGE	150mcg	ARIVEG	150 mg	ERIVEDGE	150mg
ERIVEDGE	150mg	ARIVEGE	150mg	ERIVEDGE	150 mg
ERIVEDGE	150mg	AROVEG	150 mg	ERIVEDGE	150mg
ERIVEDGE	150 mg	ERYVEG	150mg	ERIVEDGE	150 mg
ERIVEDGE	150 mg			ERIVEDGE	150 mg
				ERIVEDGE	150mg
				ERIVEDGE	150 mg
				ERIVEDGE	150mg
				ERIVEDGE	150 mg
				ERIVEDGE	150 mg

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

Proprietary Name	Active Ingredient	Similarity to Erivedge	Failure preventions
Amerge	naratriptan HCl	Look and Sound	Lacks sufficient orthographic similarity based on the following aspects of the name Amerge: appears shorter when scripted and lacks a letter providing an upstroke. Lacks sufficient phonetic similarity based on the following aspects of the name, Amerge: includes only two syllable and lacks a syllable with the beginning consonant sounds of "rr" and "vv."
Eridium *(discontinued branded generic but other similar products are marketed)*	Phenazopyridine	Look	Lacks sufficient orthographic similarity based on the following aspects of the name, Eridium: lacks a letter providing a down stroke, the shared letter 'd' appears closer to the beginning of the name, and lacks a down stroke.
	Erythromycin	Sound	Lacks sufficient phonetic similarity based on the following aspects of the name, Erythromycin: includes two additional syllables, and includes beginning consonant sounds in the third ("th"), fourth ("mm") and fifth ("ss") syllables are not heard in Erivedge.
Estinyl	ethinyl estradiol	Look	Lacks sufficient orthographic similarity based on the following aspects of the name, Estinyl: Includes the letter 't' which provides an additional upstroke and a cross stroke when scripted, the letters providing down stroke (y) and upstroke (l) appear as the final letters and in reverse order. In addition, this is a discontinued medication (1996) with no generic equivalents and does not appear in the Red Book (Active or Deactivated). The application was withdrawn in 2003, and a Federal Register notice was published in 2004.
Evista	raloxifene HCl	Look	Lacks sufficient orthographic similarity based on the following aspects of the name, Evista: appears shorter when scripted, lacks a letter providing a down stroke and includes the letter 't' which may provide a cross stroke.
Feratab	ferrous sulfate	Sound	Lacks sufficient phonetic similarity based on the following aspects of the name, Feratab: includes a beginning consonant sound "ff;' and the third and final syllable sounds different ("tab" vs. "vehdj").

Veregen	sinecatechins	Sound	Lacks sufficient phonetic similarity based on the following aspects of the name, Veregen: includes a beginning consonant sound “VV,” the similar consonant sound “jj” in the third syllable are heard at the beginning of the syllable, and the remaining consonant sounds in the third syllable differ.(“nn” vs. “vv”).

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

Proposed name: **Erivedge** **(vismodegib)** **150 mg capsules** **Usual dose: One capsule by mouth one daily**		**Other Failures to consider with this product** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* (b) (4) [redacted]
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion **Causes (could be multiple)**	**Prevention of Failure Mode(name confusion)**
Aerobid (flunisolide) 0.25 mg per inhalation metered dose inhaler Usual dose: Two inhalations by mouth twice daily (up to four inhalations per dose)	**Phonetic similarity:** Both names include three syllables, the first share the same vowel sound ("Eh"), the second syllables sound similar when spoken ("roh" vs. "ree"). Both products have a single strength presentation and are administered orally.	Phonetic difference stems from the fact that the third syllable in Aerobid begins ("bb" vs. "vv") and ends ("dd" vs. "j") with different sounding consonant sounds. Aerobid has a dose of two to four inhalations which are administered twice daily. Erivedge has a dose of one capsule administered once daily.

Aranesp (darbepoetin alfa) 25 mcg/mL, 40 mcg/mL, 60 mcg/mL, 100 mcg/mL, 150 mcg/0.75 mL, 200 mcg/mL, and 300 mcg/mL vials 150 mcg/0.75 mL and 500 mcg/1 mL syringes Other prefilled syringe strengths 25 mcg, 40 mcg, 60 mcg, 100 mcg, 200 mcg and 300 mcg. Usual dose: One syringe or vial subcutaneously or intravenously weekly, every two weeks, or every four weeks. The dose is based on weight and patient's hemoglobin level but rounded to the nearest strength.	**Phonetic similarity:** Both names include three syllable; the first two syllables of each name sound similar when spoken ("Eh-rah" vs. "Eh-ree"); and the third includes the same vowel sound ("eh"). Both products share a numeric strength and dose (150 mcg vs. 150 mg).	Phonetic difference stems from the third syllable of Aranesp which begins with the letter 'n' which provides the consonant sound "nn" and concludes with the mixed consonant sound of "sp" provided by the letters 's' and 'p.' Aranesp is an injection which is administered subcutaneously or intravenously. It is administered one time, weekly, every two weeks, or every four weeks. Erivedge is an oral capsule administered once daily.

Aricept (donepezil HCL) 5 mg, 10 mg, and 23 mg tablet, 5 mg and 10 mg orally disintegrating tablet, 1 mg/ml oral solution Usual dose: One tablet (5 mg, 10 mg or 23 mg) by mouth daily.	**Orthographic similarity:** Both names have a similar length when scripted, begin with a letter grouping that may appear similar when scripted (Ari vs. Eri), include a letter providing and upstroke (t vs. d) and one letter providing a down stroke (p vs. g) in similar positions. **Phonetic similarity:** Both names include three syllable; the first two syllables of each name sound the same when spoken ("Eh-ree"); and the third includes the same vowel sound ("eh"). Both products are oral solid dosage forms (tablet vs. capsule) which are administered once daily.	Orthographic difference stems from the fact that the letters 'p' and 't' in Aricept that provide the down stroke and upstroke, respectively appear in reverse order compared to those features in Erivedge. In addition, Erivedge includes the letter 'e' following the letters which provide the upstroke and down stroke. Phonetic different stems from the consonant sound heard in the third syllable of Aricept. The beginning sound is "ss" provided by the letter 'c' and concluding mixed consonant sound provided by the letters 'p' and 't' ("pt" vs. "j") Aricept is available in four strength presentations with three for the oral solid dosage form. Thus, a strength is necessary for a complete prescription or to order the medication. Erivedge is available as a 150 mg capsule which does not overlap with the strengths of Aricept.

Atrovent (ipratropium bromide) 0.03% and 0.06% nasal spray Usual dose: two sprays each nostril three or four times daily. 14.7 g HFA metered dose inhaler Usual dose: Inhale two inhalations by mouth four times daily. 0.02% solution for nebulization (discontinued with generics available) Usual dose: Inhale one vial (0.5 mg or 2.5 mL) via nebulizer four times daily.	**Phonetic similarity:** Both names include three syllables, the first is a vowel sound ("A" vs. "Eh"), and the third syllable begins with the same consonant and vowel sounds ("veh"). The frequency of use may appear similar (qid vs. qd).	Phonetic difference stems from the fact that Atrovent include a mixed consonant at the beginning of the second syllable "tr" and the third syllable ends with a mixed consonant sound ("nt" vs. "j"). Atrovent is available in three dosage forms. The nasal spray has two strength presentations. It is necessary to specify the inhalation dosage form if the use of a nebulizer is not mentioned. Erivedge is a 150 mg strength capsule.
Cervidil (dinoprostone) 10 mg vaginal insert Usual dose: one insert vaginally one time to induce labor.	**Orthographic similarity:** Both have a the same number of letters (eight) and a similar length when scripted, begin (C vs. E) and end (l vs. e) with letters that may appear similar when scripted and include a similar letter grouping in the name (-vid- vs. –ved-). Both are available as a single strength presentation.	Orthographic difference stem from the fact that Erivedge includes the letter 'g' which provides a down stroke. In addition, the letter 'l' may be scripted with an upstroke at the end of Cervidil. Cervidil is a vaginal insert used to induce labor after the administration of a single dose. Cervidil is stored frozen until ready to dispense. Erivedge is an oral capsule taken daily and is stored at room temperature.

Econazole (the active moiety in Spectrazole) 1% cream Usual dose: Apply sufficient amount topically to effected area once daily.	**Orthographic similarity:** both names begin and end with the same letter (E and e, respectively), have a similar length when scripted, and include letters that may provide an upstroke (l vs. d) and a down stroke (z vs. g). Both are single strength products that are administered once daily.	Orthographic difference stems from the fact that Econazole includes the down stroke and upstrokes provided by the letters 'z' and 'l' in a opposition order to the same features in Erivedge. In addition, these letters are separated by a letter (o) rather than adjacent to each other. Econazole is a topical cream available in three sizes (15 g, 30 g, and 85 g tubes). Thus, a quantity is needed for a complete prescription when written to "use as directed." Erivedge is an oral capsule available in the net quantity of 28 capsules which is not similar to the sizes of Econazole.
Erbitux (cetuximab) 100 mg/50 mL and 200 mg/100 mL vials Usual dose: 400 mg/m^2 infused intravenously over 120 minute on week 1, then 250 mg/m^2 infused intravenously over 60 minutes weekly, thereafter.	**Orthographic similarity:** Both names have a similar length when scripted, begin with the same letter pair (Er) and include a letter in the sixth position which provides and upstroke (t vs. d). Both products are chemotherapy agents.	Orthographic difference stems form the fact that Erbitux includes the letter 'b' which provides and additional upstroke and lacks a letter providing a down stroke. In addition, Erbitux includes the letter 'x' which provides a cross stroke at the end of the name. Erbitux is an injection which is infused intravenously each week in a clinical setting. The Erivedge dose of 150 mg is not achievable based on the 400 mg/m^2 and 250 mg/m^2 dosing regimens. Erivedge is a 150 mg capsule which is administered orally once a day.
Eribulin (Active moiety of Havalen) 1 mg/2 mL vial Usual dose: 1.4 mg/m^2 infused intravenously over 2 to 5 minutes weekly times two doses (Days 1 and 8) of 21 day cycle. Dose may be adjusted down to 0.7 mg/m^2 to 1.1 mg/m^2.	**Orthographic similarity:** Both names have the same number of letters (eight) and a similar length when scripted, begin with the same letter grouping (Eri-) and include a letter providing an upstroke in a similar position (l vs. d). Both are chemotherapy agents available in a single strength presentation.	Orthographic difference stems from the fact that Erivedge includes the letter 'g' which provides a down stroke. In addition, Eribulin include the letter 'b' which provides and an additional upstroke. Eribulin is an injectable product with an achievable dose range of approximately 1.1 mg to 3.1 mg. It is administered intravenously once a week in a clinical setting. Erivedge is an oral capsule available as 150 mg which is higher than achievable doses of Eribulin noted above. In addition, it is taken daily.

Ertaczo (sertaconazole nitrate) 2% cream Usual dose: Apply sufficient amount to cover effected area twice daily for four weeks.	**Orthographic similarity:** Both names begin with the same letter pair (Er), have a similar length when scripted, and include letters that may provide an upstroke (t vs. d) and a down stroke (z vs. g). Both are available in a single strength presentation.	Orthographic difference stems from the fact that in Ertaczo, the letter 't' appears closer to the beginning of the name and is separated from the letter 'z' by a letter pair (ac). In addition, the letter 'z' may be scripted without a down stroke. Ertaczo is a topical cream applied twice daily for four weeks. The cream is available in two sizes (30 g and 60 g) thus a quantity must be specified for a complete prescription when written to "use as directed." Erivedge is an oral capsule taken daily. It is available in a 28 capsule quantity.
Erwinaze (Asparaginase Erwinia Chrysanthemi) 10,000 international units for injection (vial) Usual dose: 25,000 international units/m^2 intramuscularly three times a week (Monday, Wednesday and Friday).	**Orthographic similarity:** Both names include eight letters, and begin (Erwi- vs. Erive-) and end (-ze vs. –ge) with similar letter groupings. Both are single strength chemotherapy products.	Some orthographic difference may be provided by the fact that Erivedge include the letter 'd' which provides an upstroke when scripted. In addition, Erwinaze includes the letter 'n' which may provide additional length to the name. Erwinaze is an powder for injection which is administered intramuscularly three times a week in a clinical setting. A numeric dose of 150 is not achievable as the dose is based on international units/m^2 and will be a five digit number. The product is packaged in cartons of five vials Erivedge is an oral 150 mg capsule taken daily. It is available in a 28 capsule quantity.
Erycette (erythromycin) 2% swab Usual dose: Apply to affected areas topically twice daily.	**Orthographic similarity:** Both names begin and end with the same letter pair (Er), have a similar length when scripted, and include letters provide an upstroke (t vs. d) and a down stroke (y vs. g). **Phonetic similarity:** Both names include three syllables and the first two sound the same ("Eh-reh"). Both are available as a single strength presentation.	Orthographic difference stems from the fact that Erycette includes the letter 'y' providing a down stroke in the third position rather than the letter 'g' in the seventh position in Erivedge. In addition, Erycette include a double 't' (or tt) which provides an additional upstroke and cross strokes in the name. Phonetic different stems from the consonant sound heard in the third syllable of Erycette. The beginning sound is "ss" provided by the letter 'c' and concluding consonant sound provided by the letter 't' ("t" vs. "j"). Erycette is a topical pledgette which is applied twice daily. Erivedge is an oral capsule taken once daily.

Eryped (erythromycin ethylsuccinate) 200 mg/5 mL and 400 mg/5 mL for oral suspension Usual dose (in pediatrics): 10 to 15 lbs: 200 mg/day 16 to 25 lbs: 400 mg /day 26 to 50 lbs: 800 mg/day 51 to 100 lbs:1200 mg/day over 100 lbs: 1600 mg/day The total daily dose is divided into equal doses and administered by mouth twice, three times, or four times daily.	**Phonetic similarity:** Both names include three syllables, the first and second syllables sound the same (‘Eh –ree-‘) and the third includes the same vowel sound (‘eh”). Both are oral products, and the frequency of use may appear the same (qid vs. qd)	Some phonetic difference is provided by the fact that Eryped includes the letter ‘p’ as the beginning consonant sound of the third syllable (“pp” vs. “vv”). In addition, Erivedge concludes with a consonant sound provided by the letter ‘j’ (“j”). Eryped is available in two strength presentations, Thus, the strength is necessary for a complete prescription or to order the medication. Erivedge is available as a 150 mg capsule which does not overlap with the strength of Eryped.
Evaclon (clindamycin) 10 mg/g topical foam Usual dose: Apply a sufficient amount to cover effected area topically once daily.	**Orthographic similarity:** Both names begin with the same letter (E) and include a letter grouping that appears similar when scripted (-vacl- vs. ved-). Both products have a single strength presentation and are administered once daily.	Orthographic difference stem from the fact that in Erivedge the shared similar aspects of the name are separated by a letter pair (ri). In addition, the letter pair at the end of each name appear different when scripted (-ge vs. –on). Evaclon is a topical foam available in two sizes (50 g and 100 g cans). A size or quantity is necessary for a complete prescription when written to “use as directed.” Erivedge is an oral capsule that is packaged in a quantity of 28 capsules.
Exalgo (hydromorphone HCl) 8 mg, 12 mg, and 16 mg extended-release tablets Usual dose: One tablet by mouth once daily.	**Orthographic similarity:** Both names begin with the same letter (E) and end with a letter grouping that appears similar when scripted (-lgo vs. -dge). Both are oral solid dosage forms that have an overlapping dose of one (one tablet vs. one capsule) and are administered once daily.	Orthographic differences stem form the fact that Exalgo is shorter in length when scripted. In addition, Exalgo includes the letter ‘x’ which provides a cross stroke. Exalgo is available in three strength presentations which must be specified for a complete prescription or to order the medication. Erivedge is available as a single strength (150 mg) capsule which does not overlap with the strengths of Exalgo.

Excedrin (a family or umbrella product name) (acetaminophen, aspirin, and caffeine) 250 mg/250 mg/65 mg tablets Usual dose: Two tablets every six hours as needed	**Orthographic similarity:** Both names begin with the same letter (E) and share a letter pair in the middle of the name (ed). Both are single strength oral solid dosage forms (tablets vs. capsule).	Orthographic difference stems from the fact that Erivedge includes the letter ‘g’ which provides a down stroke. In addition, Excedrin includes three letters after the letter 'd’ providing no upstroke or down strokes. Excedrin is a product family name is used in conjunction with prefix (e.g. Extra Strength) and suffix modifiers (e.g. Back Pain or Migraine) which also provide orthographic difference. The dose of Excedrin is two tablets. The dose of Erivedge is one capsule.
Exforge (amlodipine besylate and valsartan) 5 mg/160 mg, 10 mg/160 mg, 5 mg /320 mg, and 10 mg/320 mg tablet Usual dose: One tablet by mouth one daily.	**Orthographic similarity:** Both names have a similar length when scripted, begin with a similar appearing letter pair (Ex- vs. Er), include a letter providing an upstroke (f vs. d), and end with the same letter pair (-ge). Both are oral solid dosage forms (tablet vs. capsule) which have a frequency of administration of once daily. The strength of Erivedge (150 mg) may appear similar to the second ingredient strength of Exforge (160 mg.)	Orthographic difference stems from the fact that Exforge includes a letter pair (or) separating the upstroke and down stoke in the name. In addition, the letter ‘f’ appears in the third position and may be scripted with a cross stroke or a down stroke. Exforge is a combination medication available in four strength presentations. A strength is necessary and both strengths must be represented for a complete prescription or to order the medication.

Serevent (salmeterol) 50 mg per inhalation, powder for inhalation (Diskus) Usual dose: One inhalation by mouth twice daily.	**Phonetic similarity:** Both names include three syllables, the first share the same vowel sound (“Eh”), the second syllables sound the same (“ree”) and the third syllable begins with the same consonant and vowel sounds (“veh”). Both products are available as a single strength presentation. The doses may overlap (one inhalation vs. one tablet) and are administered orally.	Phonetic difference stems from the fact that Serevent begins with a consonant sound “ss” provided by the letter ‘s.’ In addition, the third syllable of Serevent ends with a mixed consonant sound (“nt” vs. “j”) provided by the letters ‘n and ‘t.’ Serevent is administered twice daily. Erivedge is taken once daily.

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/s/

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