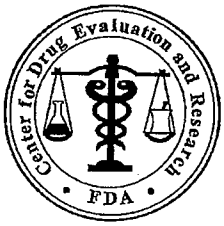
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-315

PROPRIETARY NAME REVIEW(S)



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

Date:	June 8, 2009
To:	Wiley Chambers, MD, Acting Director Division of Anti-Infective and Ophthalmologic Products
Through:	Kellie Taylor, PharmD, MPH, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Felicia Duffy, RN, BSN, MSEd, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Ozurdex (Dexamethasone Intravitreal Implant) 0.7 mg
Application Type/Number:	NDA 22-315
Sponsor:	Allergan
OSE RCM #:	2009-913

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

CONTENTS

EXECUTIVE SUMMARY

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

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

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Allergan dated May 6, 2009, for an assessment of the proposed proprietary name, Ozurdex, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

1.2 REGULATORY HISTORY

The Applicant initially submitted the proposed proprietary name, Posurdex, a December 28, 2007 IND submission. The Division of Medication Error and Prevention (DMEPA) found the name unacceptable based upon the potential for look-alike and sound-alike confusion with Precedex (see OSE review #2007-1261 dated May 14, 2009). Labeling comments were provided in OSE review #2009-339 dated June 5, 2009.

1.3 PRODUCT INFORMATION

Posurdex (dexamethasone) is a biodegradable intravitreal implant indicated for the treatment of macular edema following branch retinal vein occlusion or central retinal vein occlusion. Posurdex contains 0.7 mg dexamethasone in the Novadur™ solid polymer drug delivery system. Posurdex is preloaded into a single-use, specially designed applicator to facilitate injection of the rod-shaped implant directly into the vitreous.

An intravitreal dose of Posurdex is recommended when there is evidence of macular edema or vascular leakage in the macula. The usual dose is one intravitreal injection of 0.7 mg dexamethasone. Dosing frequency is as needed (approximately every– months). Posurdex should only be administered form a retinal specialist in their office. The intravitreal injection procedure should be carried out under controlled aseptic conditions. b(4)

Posurdex will be supplied in ' ——— containing 1 single-use plastic applicator. The ——— . will be packaged in a carton.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'O' 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 Ozurdex, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two, capital letter 'O', and lowercase 'd'), down strokes (one, lower case scripted 'z'), cross strokes (one, lower case 'x'), and dotted (none). Additionally, several letters in Ozurdex may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Ozurdex.

When searching to identify potential names that may sound similar to Ozurdex, the DMEPA staff search for names with similar number of syllables (Three), stresses (OZ-ur-dex, or oz-UR-dex), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Oz-' may sound like 'Os-' (see Appendix B). Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. The Applicant did not provide their intended pronunciation of the proprietary name in the proposed name submission and, therefore, it could not be taken into consideration.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Ozurdex Rx Study (conducted on May 21, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order : Ozurdex implant intravitreal	Ozurdex #1 For placement in the clinic
Outpatient Prescription: Ozurdex #1 For placement in clinic	

[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 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of forty names as having some similarity to the name Ozurdex.

Thirty-eight of the names were thought to look like Ozurdex. These include: [redacted], Azulix, Agulan, Orudis, Arutrin, Azactam, Ogestrel, Azilect, Oratuss, Aralast, Aridex, Demadex, Arimidex, Azedra, Avandia, Urocit-K, Ursodiol, Aralen, Aredia, Casodex, Uvadex, Ozidia, Oxedep, Urdox, Lurdex, Ovidrel, OvaRex***, [redacted], Quinidex, Azelex, Asmanex, [redacted], Efudex, Zoladex, Azasite, Ocuflox, and Orfadin. One of the names [redacted] was thought to sound like Ozurdex. The remaining name (Posurdex***) was thought to look and sound similar to Ozurdex. b(4)

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of June 4, 2009.

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 insert Ozurdex.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

DMEPA identified and evaluated a total of seventeen practitioner respondents with none of the responses overlapping with an existing name. Ten of the participants interpreted the name correctly as "Ozurdex," with correct interpretation occurring in both the inpatient and outpatient written studies. None of the written responses misinterpreted the drug name.

In the verbal studies, six responses were misspelled phonetic variations of the proposed name, Ozurdex. The seventh response in the verbal study was "Posurdex***". Posurdex was the Applicant's initial proposed proprietary name for this application. DMEPA found the proposed name unacceptable based on the potential for look-alike and sound-alike confusion with Precedex. Our primary concern with Posurdex was the potential for orthographic confusion between the two names (see OSE review #2007-1261). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION

DMEPA notified the Division of Drug Anti-Infective and Ophthalmologic Products via e-mail that we had no objections to the proposed proprietary name, Ozurdex, on June 4, 2009. Per e-mail correspondence from the Division of Anti-Infective and Ophthalmologic Products on June 4, 2009, they indicated they had no concerns with the proposed proprietary name, Ozurdex.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator did not result in additional names which were thought to look or sound similar to Ozurdex and represent a potential source of drug name confusion. Thus, we evaluated a total of forty names.

*** **Note: This is proprietary and confidential information that should not be released to the public.*****

4 DISCUSSION

Neither DDMAC nor the review Division had concerns with the proposed name.

DMEPA identified and evaluated forty names which were evaluated for their potential similarity to the proposed name, Ozurdex. Ten names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix D).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining thirty names and lead to medication errors. This analysis determined that the name similarity between Ozurdex was unlikely to result in medication errors with any of the thirty products for the reasons presented in Appendices E through L.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Ozurdex, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Ozurdex, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. The proposed name must be resubmitted for evaluation with the submission of the NDA. For questions or clarifications, please contact Darrell Jenkins, OSE Project Manager, at 301-796-0558.

6 REFERENCES

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

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

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

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

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

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

4. ***AMF Decision Support System [DSS]***

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

For the proposed proprietary name, DMEPA staff 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 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

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

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, 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 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.

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

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

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

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

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

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

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

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

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

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

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

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

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor 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 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 Sponsor. 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 Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Ozurdex	Scripted may appear as	Spoken may be interpreted as
Capital 'O'	A, C, G, U	any vowel
lower case 'o'	a, c, or u	any vowel
lower case 'z'	j, t, r, p, or y	's'
lower case 'u'	e, i, n, o, or v	any vowel
lower case 'r'	i, n, v, or z	'n'
lower case 'd'	'cl', or 'l'	't'
lower case 'e'	a, o, i, or u	Any vowel
lower case 'x'	t, or 'L'	's'

Appendix C: FDA Prescription Study Responses

Written Outpatient	**Written Inpatient**	**Verbal Prescription**
Ozurdex	Ozurdex	Osurdex
Ozurdex	Ozurdex	Oszurdex
Ozurdex	Ozurdex	Ozendex
	Ozurdex	Ozerdex
	Ozurdex	Ozerdex
	Ozurdex	Ozerdex
	Ozurdex	Posurdex

Appendix D: Names lacking convincing look-alike and/or sound alike similarities with Ozurdex

Proprietary Name	**Proprietary Name**
Arutrin	Urdox
Oratuss	Lurdex
Ursodiol	Zoladex
Aredia	Azasite
Oxedep	Ocuflox

Appendix E: Proprietary names trademarked in foreign countries

Proprietary Name	Similarity to Ozurdex	Country
[redacted]	Look	Mexico
Azulix	Look	Brazil
Agulan	Look	Indonesia
Ozidia	Look	France
[redacted]	Sound	Columbia

b(4)

Appendix F: Proprietary name for this NDA that was previously found unacceptable

Proprietary Name	Similarity to Ozurdex
Posurdex*** (Dexamethasone)	Look/Sound

Appendix G: Discontinued product due to FDA action, removal of unapproved carbinoxamine containing products as of June 6, 2006

Proprietary Name	Similarity to Ozurdex	Source
Aridex	Look	Federal Register Notice http://www.fda.gov/OHRMS/DOCKETS/98fr/E6-9033.pdf

Appendix H: Proposed proprietary name found unacceptable, NDA was approved under a different proprietary name

Proprietary Name	Similarity to Posurdex	Source	Approved as
[redacted] (Urofollitropin)	Look	DSS	Bravelle
[redacted] (Lisdexamfetamine dimesylate)	Look	DSS	Vyvanse

b(4)

*** **Note: This is proprietary and confidential information that should not be released to the public.*****

Appendix I: IND withdrawn by the Sponsor

Proprietary Name	Similarity to Ozurdex	Source
[redacted]	Look	AIMS

b(4)

Appendix J: Unapproved orphan drug

Proprietary Name	Similarity to Posurdex	Source
Azedra (Iobenguane I131)	Look	List of orphan designations http://www.fda.gov/orphan/designat/list.htm

Appendix K: Products with no numerical overlap in strength and dose with Ozurdex

Product name with potential for confusion	Similarity to Ozurdex	Strength	Usual Dose (if applicable)	Source
Ozurdex **(Dexamethasone intravitreal implant)**		**0.7 mg**	**Usual dose:** One 0.7 mg intravitreal injection as needed	Proposed Package Insert
Orudis Discontinued, generics available (Ketoprofen) capsules	Look	25 mg, 50 mg, 75 mg	25 mg to 75 mg by mouth three times a day or four times a day.	Facts & Comparisons
Azactam (Aztreonam) injection	Look	500 mg, 1 g, 2 g	500 mg to 2 g intravenously or intramuscularly every 8-12 hrs	Facts & Comparisons
Azilect (Rasagiline mesylate) tablet	Look	0.5 mg, 1 mg	0.5 mg to 1 mg by mouth once daily	Facts & Comparisons
Aralast (Alpha-proteinase inhibitor) injection	Look	400 mg	60 mg/kg intravenously once weekly	Facts & Comparisons
Demadex (Torsemide) tablets	Look	5 mg, 10 mg, 20 mg , 100 mg	5 mg to 20 mg by mouth once daily	Facts & Comparisons

Product name with potential for confusion	Similarity to Ozurdex	Strength	Usual Dose (if applicable)	Source
Ozurdex (Dexamethasone intravitreal implant)		**0.7 mg**	**Usual dose:** One 0.7 mg intravitreal injection as needed	Proposed Package Insert
Avandia (Rosiglitazone) tablets	Look	2 mg, 4 mg, 8 mg	4 mg to 8 mg by mouth once daily or in divided doses twice daily.	Facts & Comparisons
Urocit-K (Potassium citrate) extended-release tabs	Look	5 mEq, 10 mEq	30 mEq to 60 mEq by mouth in divided doses (3 or 4 times/day)	Facts & Comparisons
Asmanex (Mometasone furoate) inhaler	Look	110 mcg 220 mcg	2 puffs by mouth once or twice daily	Facts & Comparisons
Efudex (Flurouracil) cream	Look	2%, 5%	Apply to affected area twice daily	Facts & Comparisons
Orfadin (Nitisinone) caps	Look	2 mg, 5 mg, 10 mg	1-1.5 mg/kg/day by mouth in two divided doses	Facts & Comparisons
[redacted]	Look	[redacted]	[redacted]	OSE review 2006-279

b(4)

*** Note: This is proprietary and confidential information that should not be released to the public.***

Appendix L: Drug names with single strength availability but with differentiating product characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Ozurdex (Dexamethasone)		**0.7 mg**	**One 0.7 mg intravitreal implant as needed**	
Arimidex (Anastrozole) tablets	Look	1 mg	1 tab by mouth once daily	**Dosage form:** Tablet vs. implant **Route of administration:** Oral vs. ophthalmic injection **Frequency of administration:** Once daily vs. as needed
Aralen (Chloroquine phosphate) tablets	Look	500 mg	Prophylaxis: 1 tab by mouth on the same day each week Acute attack: 1 g followed by and additional 500 mg after 6-8 hrs and a single dose of 500 mg on each of two consecutive days.	**Dosage form:** Tablet vs. implant **Route of administration:** Oral vs. ophthalmic injection **Frequency of administration:** Once a week or over 3 days vs. as needed
Casodex (Bicalutamide) tablets	Look	50 mg	1 tab by mouth once daily	**Dosage form:** Tablet vs. implant **Route of administration:** Oral vs. ophthalmic **Frequency of administration:** Once daily vs. as needed **Indication:** Prostate cancer vs. macular edema
Uvadex (Methoxsalen) solution	Look	20 mcg/mL	Give extracorporeal treatment on 2 consecutive days every 4 weeks for a minimum of 7 treatment cycles	**Dosage form:** Solution vs. implant **Route of administration:** Extracorporeal vs. ophthalmic injection **Indication:** Cutaneous T-cell lymphoma vs. macular edema Additionally, Uvadex is intended for use with the UVAR or UVAR XTS photopheresis system
Ovidrel (Choriogonadotropin alfa) injection	Look	250 mcg per 0.5 mL	250 mcg subcutaneously 1 day following the last dose of follicle stimulating agent	**Dosage form:** Solution vs. implant **Route of administration:** Subcutaneous vs. intravitreal injection **Indication:** Infertility vs. macular edema

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Ozurdex (Dexamethasone)		**0.7 mg**	**One 0.7 mg intravitreal implant as needed**	
Azelex (Azelaic acid) cream	Look	20%	Apply thin film to affected area twice daily	**Dosage form:** Cream vs. implant **Route of administration:** Topical vs. intravitreal injection **Frequency of administration:** Twice daily vs. as needed **Indication:** Acne vs. macular edema
Quindex (Quinidine sulfate) extended-release tabs	Look	300 mg	1 tab by mouth BID or TID	**Dosage form:** Tablet vs. implant **Route of administration:** Oral vs. intravitreal injection **Frequency of administration:** Twice or three time daily vs. as needed **Indication:** Atrial fibrillation/flutter and ventricular arrhythmias vs. macular edema
Ogestrel (ethinyl estradiol; norgestrel) tabs	Look	0.05 mg/0.5mg	1 tab by mouth once daily	**Dosage form:** Tablet vs. implant **Route of administration:** Oral vs. intravitreal injection **Frequency of administration:** Once daily vs. as needed **Indication:** Contraception vs. macular edema

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