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RESEARCH**

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PROPRIETARY NAME REVIEW(S)

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

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Subject: Proprietary Name and Label Review

Drug Name(s) & Strength(s): Oxecta (Oxycodone HCl) Tablets 5 mg and 7.5 mg

Applicant: King Pharmaceuticals Inc.

OSE RCM #: 2011-1521 and 2011-2169

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of Oxecta as the proposed proprietary name and container labels for Oxycodone HCl Tablets. Our proprietary name evaluation did not identify concerns that would render the proprietary name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name Oxecta acceptable for this product. DMEPA will notify the Applicant of these findings via letter.

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.

Our label and labeling risk assessment indicates the presentation of information on the proposed labels and labeling introduces vulnerability to confusion that can lead to medication errors. We provide label and labeling recommendations in section 5 of this review

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from King Pharmaceuticals dated May 10, 2011 for a promotional and safety assessment of the proposed proprietary name, Oxecta. Additionally, the Applicant submitted container labels for review on June 2, 2011 which we evaluated to identify vulnerabilities that may cause confusion leading to medication errors.

1.2 PRODUCT INFORMATION

Oxecta (Oxycodone HCl) is an opioid analgesic indicated for the management of moderate to severe pain when the use of an opioid analgesic is appropriate. The usual recommended dose of Oxecta (Oxycodone HCl) is 5 to 15 mg by mouth every 4 to 6 hours as needed for pain. Oxecta (Oxycodone HCl) will be available as white round, convex tablets with the King logo on one side and with "5" debossed on the 5 mg tablets and "7.5" debossed on the 7.5 mg tablets on the other side. Oxecta will be packaged in bottles containing 100 tablets.

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letters '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}

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

To identify drug names that may look similar to Oxecta, the DMEPA safety evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), upstrokes (one, ‘t’), down strokes (none), cross strokes (two, ‘x’ and lower case ‘t’), and dotted letters (none). Additionally, several letters in Oxecta 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 Oxecta.

When searching to identify potential names that may sound similar to Oxecta, DMEPA searches for names with similar number of syllables (three), stresses (OX-ec-ta, OX-EC-ta, OX-ec-TA), and placement of vowel and consonant sounds. (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.

2.2 PRESCRIPTION ANALYSIS STUDIES

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

2.3 LABELS AND LABELING RISK ASSESSMENT

The Division of Medication Error Prevention and Analysis (DMEPA) used Failure Mode and Effects Analysis (FMEA)³ to evaluate the container labels submitted June 2, 2011. (Appendix G)

3 RESULTS

The following sections describe the findings from our database searches, expert panel discussion, prescription analysis studies and safety evaluator risk assessment.

3.1 DATA BASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of 23 names as having some similarity to the name Oxecta.

Twenty one names were thought to look like Oxecta. They are: Oxistat, Ogestrel, Azactam, Promacta, Oxymeta 12, Oxyfrin, Oxytrex, Umecta, Orvaten, Oretic, Ovide, Dicoto, Ocella, (b) (4) Oxeda, Axocet, Ocuville and Oforta. Two of the names, Expecta and Oxepa were thought to look and sound like Oxecta.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of June 3, 2011.

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

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

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 Oxecta.

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

3.3 PRESCRIPTION ANALYSIS STUDIES

A total of 26 practitioners responded to the prescription analyses studies and none of the responses overlap with existing marketed products. In the written prescription study, all of the participants (n=16) interpreted the scripted name sample correctly. In the verbal studies, five (n=5) out of ten participants interpreted the name correctly. Please note that some participants in the study did not provide answers for all samples. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 SAFETY EVALUATOR SEARCHES

Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look or sound similar to Oxecta and represent a potential source of drug name confusion.

Therefore, we evaluated a total of 23 names identified in section 3.1 above.

3.5 COMMENTS FROM THE DIVISION OF ANESTHESIA, ANALGESIA AND ADDICTION PRODUCTS (DAAAP)

3.5.1 Initial Phase of Review

In response to the OSE, May 20, 2011 e-mail, DAAAP did not forward any concerns on the proposed name at the initial phase of the name review.

3.5.2 Midpoint of Review

DMEPA notified DAAAP via e-mail that we had no concerns with the proposed proprietary name, Oxecta, on May 31, 2011. Per e-mail correspondence from DAAAP on June 3, 2011, they indicated the Division had no comments regarding the proposed proprietary trade name, Oxecta for Oxycodone HCl.

3.6 LABEL RISK ASSESSMENT

Our assessment of the container labels submitted by the Applicant has identified vulnerabilities that could lead to medication errors. We also evaluated our recommendations made in OSE Review #2011-72.

3.6.1 Container Labels

Our label risk assessment identified needed improvement in the following areas:

A. 5 mg and 7.5 mg Container Labels

1. Reduce the size and prominence of the King Pharmaceuticals symbol so that it does not compete with that of the proprietary name, established name, strength presentation, or net quantity statement.

2. Revise the statement (b) (4) to read “Oxecta tablets are to be swallowed whole and are not to be administered via nasogastric or any other feeding tubes”

4 DISCUSSION

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 their comments accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and DAAAP concurred with the findings of DDMAC’s promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

DMEPA identified 23 names for their potential similarity to the proposed name, Oxecta. We did not identify any other aspects of the name that would be considered as a potential source for error.

Eleven (n=11) of the twenty three potentially similar names did not undergo failure mode and effect analysis (FMEA) for the reasons listed in Appendix D.

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining twelve (n=12) names and lead to medication errors. This analysis determined that the name similarity between Oxecta and all of the identified names was unlikely to result in medication error for the reasons presented in Appendices E and F.

5 CONCLUSIONS AND RECOMMENDATIONS

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

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.

Additionally, our label review noted areas of needed improvement in order to minimize the potential for medication errors. We request the recommendations for the container labels be communicated to the Applicant prior to approval. See section 5.1.2 below.

If you have further questions or need clarifications, please contact Danyal Chaudhry, OSE Project Manager, at 301-796-3813.

5.1 COMMENTS TO THE APPLICANT

5.1.1 Proprietary Name Risk Assessment

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

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.

5.1.2 Labels and Labeling

Our label and labeling risk assessment identified needed improvement in the following areas:

A. 5 mg and 7.5 mg Container Labels

1. Reduce the size and prominence of the King Pharmaceuticals symbol so that it does not compete with that of the proprietary name, established name, strength presentation, or net quantity statement.
2. Revise the statement (b) (4)
 “Oxecta tablets are to be swallowed whole and are not to be administered via nasogastric or any other feeding tubes.”

6 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

7. ***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

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 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.⁴

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 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.⁵ 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.⁶ 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

⁴ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁵ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

⁶ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

name of existing and proposed drug products because similarly 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 Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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.⁷ 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 possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

⁷ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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 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 Applicant 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 Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. 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 Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant 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 Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Oxecta	Scripted may appear as	Spoken may be interpreted as
Upper case 'O'	Q, D, A	Any vowel
Lower case 'o'	a, c, e, u	
Lower case 'x'	a, d, f, n, p, r, t, v, y	Ks, kz, s, z
Lower case 'e'	a, i, l, p	Any vowel
Lower case 'c'	a, e, i, l	Z, k, s (since followed by a vowel)
Lower case 't'	r, f, x, a, l	d
Lower case 'a'	el, ci, cl, d, o, u	Any vowel

Appendix C: FDA Prescription Study for Oxecta

Figure 1. Oxecta Study Samples (conducted on May 24, 2011)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Medication Order</u></p> <p><i>Oxecta 7.5mg PO q 4h prn</i></p> <hr/> <p><u>Outpatient Rx</u></p> <p><i>Oxecta 5mg 1-2 tablets PO Q4-6° prn #360</i></p>	<p>Oxecta 5 mg tablets</p> <p>1-2 tablets by mouth every 4 to 6 hours as needed</p> <p>#360</p>

Table 1: Responses to Prescription Study

Outpatient Prescription	Inpatient Medication Order	Voice Prescription
Oxecta	Oxecta	Ocsecta
Oxecta	Oxecta	Oxacta
Oxecta	Oxecta	Oxcekta
Oxecta	Oxecta	Oxecta
		Oxseta
		Oxzecta

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 Oxecta	Failure preventions
Promacta	Eltrombopag	Orthographic	Product lacks convincing orthographic and/or phonetic similarities to Oxecta
Oxymeta 12	Oxymetazoline	Orthographic	Product lacks convincing orthographic and/or phonetic similarities to Oxecta
Oxyfrin	Oxymetazoline	Orthographic	Product lacks convincing orthographic and/or phonetic similarities to Oxecta
Oxytrex	Oxycodone and Naltrexone	Orthographic	Product lacks convincing orthographic and/or phonetic similarities to Oxecta
Ogestrel	Norgestrel and Ethinyl Estradiol	Orthographic	Product lacks convincing orthographic and/or phonetic similarities to Oxecta

(b) (4)



Axocet	Butalbital/Acetaminophen	Orthographic	Name discontinued, product is still available as Phrenelin Forte Capsules and Bupap, Cephadyn, Promacet, and Sedapap tablets. Preliminary use data indicates very low use of the name Axocet.
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Oxeda	Anastrozole	Orthographic	Foreign proprietary name only marketed in Germany.
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Appendix E: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Oxecta	Strength and Dosage Form	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Oxecta (Oxycodone)	N/A	5 mg, 7.5 mg tablets	5-15 mg by mouth every 4-6 hours as needed (one to three tablets)	N/A
Oxistat (Oxiconazole)	Orthographic	1% topical cream	1 application every 12 to 24 hours.	<p>Orthographic differences in the names, as well as differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Orthographic:</u> <i>Oxistat has two upstrokes, including one at the end of the name, whereas Oxecta only contains one.</i></p> <p><u>Dosage Form:</u> <i>Oxecta is a tablet whereas Oxistat is a topical cream.</i></p> <p><u>Route:</u> <i>Oxecta is an oral medication whereas Oxistat is for topical administration.</i></p> <p><u>Strength:</u> <i>Oxistat is a 1% topical solution whereas Oxecta is a 5 mg or 7.5 mg oral tablet.</i></p>

Product name with potential for confusion	Similarity to Oxecta	Strength and Dosage Form	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Oxecta (Oxycodone)	N/A	5 mg, 7.5 mg tablets	5-15 mg by mouth every 4-6 hours as needed (one to three tablets)	N/A
Azactam (Aztreonam)	Orthographic	500 mg powder for injection, 1 gram powder and premixed solution for injection, 2 gram powder and premixed solution for injection	1 to 2 grams IV every 6 to 12 hours	<p>Differences in product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Dosage Form:</u> <i>Aztreonam is an intravenous preparation (powder or premixed solution for injection) whereas Oxecta is a tablet.</i></p> <p><u>Route:</u> <i>Aztreonam is administered intravenously whereas Oxecta is administered orally.</i></p> <p><u>Strength:</u> <i>Azactam is available as 500 mg, 1 gram, or 2 gram powder/solution for injection whereas Oxecta is a 5 mg or 7.5 mg oral tablet.</i></p>
Ovide (Malathion)	Orthographic	0.5% topical lotion	Apply to hair and scalp to saturate. Leave on for 8-12 hours, then shampoo.	<p>Differences in product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Dosage Form:</u> <i>Ovide is a topical lotion whereas Oxecta is a tablet.</i></p> <p><u>Route:</u> <i>Ovide is for topical administration to the hair and scalp whereas Oxecta is an oral tablet.</i></p> <p><u>Dosing:</u> <i>Ovide is administered in a single dose to the scalp/hair; Oxecta is an oral tablet dosed every 4 to 6 hours as needed.</i></p>

Product name with potential for confusion	Similarity to Oxecta	Strength and Dosage Form	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Oxecta (Oxycodone)	N/A	5 mg, 7.5 mg tablets	5-15 mg by mouth every 4-6 hours as needed (one to three tablets)	N/A
Dicoto (Docusate)	Orthographic	50 mg/5 mL oral solution	<p>Adult: 50-300 mg daily in single or divided doses.</p> <p>Peds: 25-150 mg daily in single or divided (twice daily) doses</p>	<p>Differences in product characteristics, along with orthographic differences, minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Orthographic:</u> <i>Oxecta contains a cross stroke (x) in the second position, where as Dicoto does not.</i></p> <p><u>Strength:</u> <i>Dicoto is a 50 mg/5 mL oral solution, whereas Oxecta is a 5 mg or 7.5 mg oral tablet.</i></p>
Ocella (Drospirenone/Ethinyl Estradiol)	Orthographic	3 mg/0.03 mg	1 tablet daily	<p>Differences in product characteristics, along with orthographic differences, minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Orthographic:</u> <i>Ocella contains two upstrokes (ll) whereas Oxecta contains only one.</i></p> <p><u>Dose:</u> <i>Oxecta requires a strength when prescribed whereas Ocella is a single strength product. None of the product strengths overlap.</i></p> <p><u>Frequency:</u> <i>Oxecta is dosed every 4 to 6 hours as needed, whereas Ocella is dosed once daily.</i></p>

Product name with potential for confusion	Similarity to Oxecta	Strength and Dosage Form	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Oxecta (Oxycodone)	N/A	5 mg, 7.5 mg tablets	5-15 mg by mouth every 4-6 hours as needed (one to three tablets)	N/A
Ocuville (Multiple Vitamin)	Orthographic	Single strength	1 tablet daily	<p>Differences in product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Dose:</u> <i>Oxecta requires a strength when prescribed, whereas Ocuville is a single strength product. None of the product strengths overlap.</i></p> <p><u>Frequency:</u> <i>Ocuville is a once daily medication, whereas Oxecta is dosed every 4 to 6 hours as needed.</i></p>
Oforta (Fludarabine)	Orthographic	10 mg	<p>40 mg/m² daily days 1-5, for 1 week out of every 4, rounded to the nearest mg.</p> <p>Dosage for 1.73 m² adult= 70 mg (rounded to nearest 10 mg)</p>	<p>Differences in product characteristics, along with orthographic differences, minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Orthographic:</u> <i>Oforta has an upstroke and/or downstroke in the second position, depending on how the letter f is scripted, whereas Oxecta has a cross stroke (x) in the second position.</i></p> <p><u>Frequency:</u> <i>Oxecta is dosed every 4 to 6 hours as needed, whereas Oforta is a once daily dose.</i></p> <p><u>Dose:</u> <i>Oforta is dosed based upon body surface area. The dose is 40 mg per meter squared of body surface area therefore, it is highly unlikely that a dose would be less than four tablets given once daily. Oxecta is dosed as five to fifteen mg, or one to three tablets given up to six times per day.</i></p>

Product name with potential for confusion	Similarity to Oxecta	Strength and Dosage Form	Usual Dosage and Administration	Name confusion is prevented by the combination of stated product characteristics, orthographic, and/or phonetic differences as described.
Oxecta (Oxycodone)	N/A	5 mg, 7.5 mg tablets	5-15 mg by mouth every 4-6 hours as needed (one to three tablets)	N/A
Oretic (Hydrochlorothiazide)	Orthographic	25 mg	12.5- 25 mg (one to two tablets) daily	Differences in product characteristics minimize the likelihood of medication error in the usual practice setting. <u>Frequency:</u> <i>Oretic is dosed once daily whereas Oxecta is dosed every 4 to 6 hours as needed.</i> <u>Strength:</u> <i>Oxecta is available as 5 mg and 7.5 mg tablets, whereas Oretic is only available as 25 mg tablets.</i>

Appendix F: Risk of medication errors due to product confusion minimized by dissimilarity of the names or specified product characteristics

Proposed name: Oxecta (Oxycodone)	Strength and Dosage Form: 5 mg, 7.5 mg Tablets	Usual Dose: 5-15 mg by mouth every 4-6 hours as needed (one to three tablets)
Failure Mode: Name confusion	Causes	Prevention of Failure (name confusion) Leading to a Medication Error
Umecta (Urea) <u>Strength and Dosage Form:</u> 40% nail film suspension, topical emulsion, topical mousse, topical suspension, topical bioadhesive emulsion, and topical bioadhesive suspension <u>Dose:</u> Apply to affected areas twice daily	Orthographic Similarities: Umecta and Oxecta both end in -ecta, and the letter U is orthographically similar to the letter O when scripted.	Differences in product characteristics minimize the likelihood of medication error in the usual practice setting. Rationale: Umecta is a single strength, topical urea preparation available in multiple dosage forms. It is dosed twice per day. The dosage form would need to be indicated when prescribed, and Umecta shares no overlapping doses with Oxecta. Therefore, with a different route of administration, need to specify dosage form, and no overlapping doses, the likelihood of error with Umecta and Oxecta is low.

Proposed name: Oxecta (Oxycodone)	Strength and Dosage Form: 5 mg, 7.5 mg Tablets	Usual Dose: 5-15 mg by mouth every 4-6 hours as needed (one to three tablets)
Failure Mode: Name confusion	Causes	Prevention of Failure (name confusion) Leading to a Medication Error
<p>Expecta (Docosahexaenoic Acid (DHA))</p> <p><u>Strength and Dosage Form:</u> 200 mg softgel capsule</p> <p><u>Dose:</u> One capsule daily</p>	<p>Orthographic Similarities: Both names have letters which can be scripted ambiguously at the beginning of the name (ex vs. ox), as well as the same ending of the name -ecta.</p> <p>Phonetic Similarities: Both names begin with a vowel and “x” (ex vs. ox) and end in the same letter string, -ecta.</p> <p>Overlap in Route: Both products are taken orally</p>	<p>Differences in product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p>Rationale: Expecta is a single strength product, whereas Oxecta contains multiple strengths, none of which overlap with Expecta. Expecta also contains a downstroke (p) in the middle portion of the name, whereas Oxecta contains no downstrokes in the name. Expecta is dosed once daily whereas Oxecta is dosed every 4 to 6 hours as needed. Therefore, with differences in strength, orthographic differences as well as differences in dosing frequency the likelihood of error in the usual practice setting with Oxecta and Expecta is low.</p>
<p>Orvaten (Midodrine)</p> <p><u>Strength and Dosage Form:</u> 2.5 mg, 5 mg, 10 mg tablets</p> <p><u>Dose:</u> 10 mg three times daily</p>	<p>Orthographic Similarities: Orv- and Oxe- can appear similar when scripted</p> <p>Overlap in Dose: Both products have 10 mg doses</p> <p>Overlap in Route: Both products are taken orally</p> <p>Overlap in Strength/Dosage Form/Frequency: Both products contain a 5 mg tablet strength and can be prescribed as every 6 hours</p>	<p>Orthographic differences minimize the likelihood of medication error in the usual practice setting.</p> <p>Rationale: Orvaten is a proprietary name for Midodrine. The infix “rva” elongates the name Orvaten which appears longer than Oxecta when scripted, therefore providing orthographic difference. Preliminary use data indicates that the name Orvaten is rarely used in prescribing, therefore, the likelihood of error in the usual practice setting with Orvaten and Oxecta is low.</p>

Proposed name: Oxecta (Oxycodone)	Strength and Dosage Form: 5 mg, 7.5 mg Tablets	Usual Dose: 5-15 mg by mouth every 4-6 hours as needed (one to three tablets)
Failure Mode: Name confusion	Causes	Prevention of Failure (name confusion) Leading to a Medication Error
<p>Oxepa (Nutrition for tube feeding for patients with Sepsis, Acute Respiratory Distress Syndrome (ARDS) and Acute Lung Injury (ALI))</p> <p><u>Strength:</u> Single strength</p> <p><u>Dose:</u> Personalized per patient</p>	<p>Orthographic Similarities: Both names begin with the letter string Oxe-</p>	<p>Differences in product characteristics minimize the likelihood of medication error in the usual practice setting.</p> <p>Rationale: Oxepa is a single strength nutritional product for use in acute care settings for patients with Sepsis, ARDS or ALI. It is administered via tube feeding, and is available in 1 liter ready to hang bottles or 8 ounce ready to feed cans, whereas Oxecta is an oral tablet that is available in multiple strengths. Oxepa also contains a downstroke in the fourth position, whereas Oxecta contains no downstrokes in the name. Therefore, with differences in strength, and dosage form, as well as orthographic differences, the likelihood of error in the usual practice setting with Oxecta and Oxepa is low.</p>

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/s/

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