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RESEARCH**

APPLICATION NUMBER:

204031Orig1s000

PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date: October 1, 2013

Reviewer: Vicky Borders-Hemphill, Pharm.D.
Division of Medication Error Prevention and Analysis

Team Leader: Jamie Wilkins Parker, Pharm.D.
Division of Medication Error prevention and Analysis

Drug Name and Strength: Xartemis XR
(oxycodone hydrochloride and acetaminophen)
Extended Release Tablets 7.5 mg/325 mg

Application Type/Number: NDA 204031

Applicant/Sponsor: Mallinckrodt Inc.

OSE RCM #: 2013-1717

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1 INTRODUCTION

1.1 REGULATORY HISTORY

On May 28, 2013, Mallinckrodt Inc. submitted an NDA for Xartemis XR (oxycodone hydrochloride and acetaminophen) Extended Release Tablets for the management of [REDACTED] (b) (4) acute pain. On July 18, 2013, the Applicant submitted a request for DMEPA to review the proposed proprietary name, Xartemis. On August 5, 2013, DMEPA met with Mallinckrodt, Inc. via teleconference to convey that the name Xartemis was found to be unacceptable during preliminary review due to the lack of a modifier appended to the name to indicate the extended-release properties of the drug. Mallinckrodt, Inc. submitted the name, Xartemis XR, on August 23, 2013.

This review evaluates the proposed proprietary name, Xartemis XR (oxycodone hydrochloride and acetaminophen) Extended Release Tablets, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A.

1.2 PRODUCT INFORMATION

The following product information is provided in the insert labeling submitted August 23, 2013:

- Established name: oxycodone hydrochloride and acetaminophen
- Indication of Use: the management of [REDACTED] (b) (4) acute pain
- Route of administration: oral
- Dosage Form: extended release tablets
- Strength: fixed dose combination 7.5 mg OC/325 mg APAP
- Dose: two tablets every 12 hours (maximum 4 tablets or 30 mg/1300 mg daily)
- How Supplied and Container/Closure System: 100 tablets/bottle and 10 tablets per blister card; 10 cards per carton; 100 tablets/carton
- Storage: 25°C (77°F)
- Applicant: Mallinckrodt Inc.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name, Xartemis XR, is acceptable from a promotional perspective. DMEPA and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The July 25, 2013 search of the United States Adopted Name (USAN) stems identified the USAN stem, “arte-”, contained in the name Xartemis, which is designated for anti-malarials. The infix inclusion of this stem does not represent a significant regulatory conflict as the stem “arte-” is designated for the prefix position.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Xartemis XR, has no derivation or intended meaning. This proprietary name is comprised of two components: 1) the proposed root name, Xartemis, and 2) a modifier, XR. The modifier ‘XR’ has been added to the proprietary name to highlight the extended release properties of the proposed drug product. We evaluate this modifier in section 2.2.6.

2.2.3 FDA Name Simulation Studies

Xartemis

Seventy-three practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Twenty-seven of the participants interpreted the name correctly as “Xartemis”, with correct interpretations occurring in the inpatient and outpatient written prescription studies. Although there were no correct interpretations in the Voice study, all received responses were appropriate phonetic interpretations of the name and will be considered in the safety review of the name.

Xartemis XR

Forty-four practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Thirty-two of the participants interpreted the name correctly as “Xartemis XR”, with correct interpretations occurring in the inpatient and outpatient written prescription studies and the voice study. All other responses received were appropriate phonetic interpretations of the name and will be considered in the safety review of the name.

DMEPA considered various misinterpretations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 31, 2013 e-mail, DAAAP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name. These variations were used in the search for names similar to Xartemis XR.

Table 1a lists the names with potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Xartemis identified by the primary reviewer, the Expert Panel Discussion (EPD), other review disciplines, the FDA Prescription Simulation, and (b) (4).

Table 1b lists the names with potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Xartemis XR identified by the primary reviewer, the EPD, other review disciplines, and the FDA Prescription Simulation.

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

Table 1a: Collective List of Potentially Similar Names to Xartemis (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and (b) (4) External Name Study)

Look Similar to Xartemis					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
(b) (4)	FDA	(b) (4)	FDA	Xerese	FDA
Dur-Tann DM	FDA	(b) (4)	FDA	Xiaflex	FDA
Fertinex	FDA	(b) (4)	FDA	XiraTuss	FDA
Kerlone	FDA	Vertavis	FDA	(b) (4)	FDA
Latisse	FDA	Xalkori	FDA	Xtramins	FDA
Lotemax	FDA	Xanafide	FDA	Xuriden	FDA
(b) (4)	FDA	Xartemis	FDA	(b) (4)	FDA
Ventavis	FDA	Xenaderm	FDA	(b) (4)	FDA
				Zostavax	FDA
Look and Sound Similar to Xartemis					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Arimidex	External	Letairis	External	Zestril	External
Artemether	External	Xalatan	Both	Zetia	External
Artemisinin	External	Xanax	Both	Zofran	External
Arthrotec	External	Xanthene	External	Zolpidem	External
Artiss	External	Xarelto	Both	Zostrix	External
Exalgo	External	Zarontin	External	Zosyn	External
				Zyrtec	External

Table 1b: Collective List of Potentially Similar Names to Xartemis XR (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies)

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Duratriamet	FDA	Xadosin	FDA	Zortress	FDA
Verotin GR	FDA	(b) (4)	FDA		

2.2.6 Evaluation of the Modifier XR

We requested the Applicant include a modifier to highlight the extended-release properties of the product.¹

The applicant chose the modifier XR. According to ISMP's List of Products with Drug Name Suffixes, the modifier "XR" has been used for other modified-release dosage formulations to distinguish the dosing schedule from currently marketed immediate release formulations, and has been used to signal an "every 12 hour" or "twice daily" dosing schedule while others have a "once daily" dosing schedule. This product is dosed every 12 hours; therefore, the use of the modifier "XR" is consistent with the dosing frequency associated with XR. We are not aware of any errors relating to misinterpretation of "XR". Thus, we find the use of this modifier to be appropriate.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to DAAAP via a team meeting and e-mail on July 25, 2013 and September 18, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DAAAP on July 25, 2013, they stated no additional concerns with the proposed proprietary name, Xartemis. At the team labeling meeting on September 19, 2013, they stated no additional concerns with the proposed proprietary name, Xartemis XR.

3 CONCLUSIONS

The proposed proprietary name, Xartemis XR, is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Vaishali Jarral, project manager, at 301-796-4248.

4 REFERENCES

1. Micromedex Integrated Index

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

¹ Memorandum of Teleconference for IND 104702 and NDA 204031, Xartemis (Oxycodone Hydrochloride/Acetaminophen) Extended Release Tablets dated August 5, 2013. DARRTS Advice/Information Request.

algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

9. *Natural Medicines Comprehensive Databases* (www.naturaldatabase.com)

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

10. *Access Medicine* (www.accessmedicine.com)

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison’s Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman’s The Pharmacologic Basis of Therapeutics.

11. USAN Stems (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)

USAN Stems List contains all the recognized USAN stems.

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

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

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

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

14. Medical Abbreviations (www.medilexicon.com)

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

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

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

16. Walgreens (www.walgreens.com)

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

17. Rx List (www.rxlist.com)

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

18. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

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

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

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy,

minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.²

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

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

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

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

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 2. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	Considerations when Searching the Databases		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
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/Similar shape 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, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Simulation Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ 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

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

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

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

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

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

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

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name Xartemis XR	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'X'	d, f, K,P, t, U, V, Y, L, S	KS, KZ, S, Z, D
Lower case "x"	a, d, skinny f, k, n, p, r, t, v, y	ks, kz, s, z, d
Lower case 'a'	el, ci, cl, d, o, u	Any Vowel
Lower case "r"	s, n, e, v, i	
Lower case "t"	r, f, x, A	d
Lower case 'e'	a, i, l, o, u,p	Any Vowel
Lower case 'm'	m, mn, n, v, w, wi, vi, onc, z	
Lower case 'i'	e, l, c	y
Lower Case 's'	G, 5, g, n, r	x
Capital 'X'	d, f, K,P, t, U, V, Y, L, S	S
Capital 'R'	B, Pr, K	
Letter strings in Name Xartemis XR	Scripted May Appear as	Spoken May Be Interpreted as
ar	iu	
te	b, h	
mis	nus	mus, mous, nis, mist, mnys, meth, mess

Appendix C: Prescription Simulation Samples and Results

Figure 1. Xartemis Study (Conducted on June 7, 2013)

Verbal Prescription: “Xartemis two tablets twice daily dispense # 20”

Handwritten Requisition:

Medication Order:

Xartemis 2 tablets po every 12 hours

Outpatient Prescription:

Xartemis
2 tab BID
#20

Figure 2. Xartemis XR Study (Conducted on September 6, 2013)

Verbal Prescription: “Xartemis XR two tablets twice daily dispense # 20”

Handwritten Requisition:

Medication Order:

Xartemis XR 2 tablets po every 12 hours

Outpatient Prescription:

Xartemis XR
2 tab PO BID
#20

Study Name: Xartemis XR
 190 People Received Study
 44 People Responded

	13	11	20	
Total				
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
XANTERMIS XR	1	0	0	1
XARTEMIS XR	11	2	19	32
XARTENIS XR	0	0	1	1
XAVTEMIS XR	1	0	0	1
ZARTEMIS XR	0	1	0	1
ZARTENIS XR	0	1	0	1
ZARTIMEF XR	0	1	0	1
ZARTIMIS XR	0	1	0	1
ZARTIMUS SR	0	1	0	1
ZARTIMUS XR	0	3	0	3
ZYRTEMIS XR	0	1	0	1

Appendix D.1: Proprietary names not likely to be confused with Xartemis or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Xartemis	Failure preventions
1	Arimidex	anastrozole	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences
2	Artemether	artemether	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences
3	Arthrotec	diclofenac sodium, misoprostol	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences
4	(b) (4)			
5	Exalgo	hydromorphone hydrochloride	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences

No.	Proprietary Name	Active Ingredient	Similarity to Xartemis	Failure preventions
6	(b) (4)			
7				
8				
9				

No.	Proprietary Name	Active Ingredient	Similarity to Xartemis	Failure preventions
10	Vertavis	veratrum viride root	Orthographic	Withdrawn FR effective 11/05/1992 NDA 005691. No generics available.
11	Xanafide	Amonafide L-malate	Orthographic	Pair have sufficient orthographic differences. Product was listed in Orphan drugs designations and approvals as designated/withdrawn and not FDA approved for orphan indication
12	XiraTuss	carbetapentane tannate/chlorpheniramine tannate/phenylephrine tannate	Orthographic	Per Hawthorne Pharmaceuticals, the product was discontinued over 5 years ago as a business decision. There were no sales data since year 2009. There are no generic formulations available.
13				(b) (4)
14				
15				
16	Zestril	lisinopril	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences

No.	Proprietary Name	Active Ingredient	Similarity to Xartemis	Failure preventions
17	Zolpidem	zolpidem tartrate	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences
18	Zosyn	piperacillin sodium, tazobactam sodium	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences
19	Zyrtec	cetirizine hydrochloride	Orthographic and Phonetic	Pair have sufficient orthographic and phonetic differences

Appendix D.2: Proprietary names not likely to be confused with Xartemis XR or not used in usual practice settings for the reasons described.

No.	Proprietary Name	Active Ingredient	Similarity to Xartemis XR	Failure preventions
1	Duratrimet		Orthographic	International brand name for sulfamethoxazole/trimethoprim
2	Verotin GR	prenatal multivitamin and multimineral with Iron	Orthographic	Pair have sufficient orthographic differences
3	Xadosin		Orthographic	International brand name for doxazosin

Appendix E.1: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Artemisinin (Sweet Annie or sweet wormwood)</p> <p>An herbal drug; dietary supplement; antimalarial</p> <p>Strength: 100 mg or 200 mg</p> <p>Dosage form: capsule or tea or gel</p> <p>Dose: 1 or 2 capsules or 5 to 9 grams in one liter of water one or two times daily before meals</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with letters that may appear similar when scripted “X” vs. “A”.</p> <p>Both names contain the following letters in order “rtemis”</p> <p>Phonetic similarities:</p> <p>Both products contain the string of letters “artemis”</p> <p>Overlapping Product Characteristics:</p> <p>Frequency: every twelve hours vs. twice daily</p> <p>Route: oral</p>	<p>Orthographic Differences:</p> <p>The name artemisinin has the suffix “inin” at the end of the name providing for orthographic elongation vs. Xartemis</p> <p>Phonetic differences:</p> <p>The name artemisinin has two additional syllables at the end of the name “inin” vs. xartemis</p> <p>Product Characteristic Differences:</p> <p>Strength: Xartemis has a single strength which may be omitted vs. Artemisinin has two strengths which must be included on the prescription</p> <p>Dosage form: Xartemis has a single dosage form which may be omitted vs. Artemisinin has several dosage forms which must be included on the prescription</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Artiss (fibrinogen, aprotinin, calcium chloride, thrombin) fibrin sealant for skin-graft adhesion</p> <p>Strength: N/A</p> <p>Pack size: 2 mL, 4 mL, 10 mL</p> <p>Dosage form: frozen solution in pre-filled syringe and lyophilized powder for solution</p> <p>Dose: 2 mL will cover approximately 100 cm² surface area. Apply as a thin layer using the Easyspray and Spray Set</p> <p>Route of Administration: topical</p>	<p>Orthographic similarity: Both names begin with letters that may appear similar when scripted “Xarti” vs. “Arti”</p> <p>Phonetic similarities: Both names begin with prefixes that may sound similar “Xart” vs. “Art” and end with suffixes that may sound similar “mis” vs. “tiss”</p> <p>Overlapping Product Characteristics: Strength: Xartemis has single strength which may be omitted from the prescription vs. Artiss is combined product with no strength expression</p> <p>Dose: Xartemis may be expressed as “2 tablets” and Artiss may be expressed as “2 mL”</p>	<p>Orthographic Differences: The prefix “Xar” has the extra letter “X” in the prefix and the suffix “emis” is orthographically elongated vs. “iss”</p> <p>Phonetic differences: The name Xartemis has 3 syllables (includes infix “tem”) vs. Artiss has 2 syllables</p> <p>Product Characteristic Differences: Frequency: Xartemis is every 12 hours vs. Artiss may be “use as directed” or “once”</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Dur-Tann DM (Dextromethorphan/Phenylephrine/Brompheniramine)</p> <p>Strength: 8 mg/20 mg/ 20 mg per 5 mL</p> <p>Dosage form: suspension</p> <p>Dose: Adults: 10 mL every 4 hours Pediatrics 6-11 years: 5 mL every 4 hours</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity: Both names begin with prefixes that may appear similar when scripted “Xart” vs. “Durt” and have suffices that may appear similar when scripted “emis” vs. “ann”</p> <p>Both names have similar shape.</p> <p>Overlapping Product Characteristics: Strength: Both products have a single strength which may be omitted from the prescription</p> <p>Route of administration: oral</p>	<p>Product Characteristic Differences: Dose: Xartemis is expressed in “mg” or “2 tablets” and DurTann is expressed in “mL” or “teaspoons”</p> <p>Frequency: Xartemis is every 12 hours vs. Dur-Tann DM every 4 hours</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Fertinex (Urofollitropin)</p> <p>Strength: 150 IU/amp and 75 IU/amp</p> <p>Dosage form: powder for injection solution</p> <p>Dose: 150 IU intramuscularly or subcutaneously daily until adequate follicular development (~10 days) or initially 75 IU IM or SC daily</p> <p>Route of Administration: intramuscular and subcutaneous</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xart” vs. “Fert” and have suffices that may appear similar when scripted “emis” vs. “inex”</p> <p>Both names have similar shape and length.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: 7.5 mg vs. 75 IU</p>	<p>Product Characteristic Differences:</p> <p>Dose: Xartemis is expressed in “mg” or “2 tablets” and Fertinex is expressed in “IU”</p> <p>Route of administration: Xartemis oral which may be omitted vs. Fertinex intramuscularly or subcutaneously which must be included</p> <p>Frequency: Xartemis is every 12 hours (there is no dose adjustment in proposed insert for renal or hepatic insufficiency) vs. Fertinex is once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Kerlone (Betaxolol)</p> <p>Strength: 10 mg and 20 mg</p> <p>Dosage form: tablet</p> <p>Dose: usual is 10 mg daily or 20 mg daily or 5 mg once daily in elderly and in renal failure</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xart” vs. “Kerl” and have suffices that may appear similar when scripted “emis” vs. “one”</p> <p>Both names have similar shape and length.</p> <p>Overlapping Product Characteristics:</p> <p>Route of administration: oral</p>	<p>Product Characteristic Differences:</p> <p>Strength: Xartemis has a single strength which may be omitted from the prescription vs. Kerlone has two strengths which must be included. There are no overlapping strengths</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Kerlone is once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Latisse (bimatoprost)</p> <p>Strength: 0.03%</p> <p>Dosage form: solution</p> <p>Dose: Apply nightly directly to the skin of the upper eyelid margin at the base of the eyelashes using the accompanying applicators. Blot any excess solution beyond the eyelid margin. Dispose of the applicator after one use. Repeat for the opposite eyelid margin using a new sterile applicator</p> <p>Route of Administration: ophthalmic</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xa” vs. “La”. The letters “temis” may appear similar to the letters “tisse” when scripted</p> <p>Both names have similar shape.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both products have single strength which may be omitted from the prescription</p>	<p>Orthographic Differences:</p> <p>Xartemis prefix contains the letter “r” before the upstroke letter “t” elongating the Xartemis prefix vs. Latisse</p> <p>Product Characteristic Differences:</p> <p>Dose: Xartemis is expressed as “2 tablets” and Latisse may be expressed as “apply” or “one application”</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Latisse is once nightly or “use as directed”</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Letairis (ambrisentan) Pulmonary hypertension</p> <p>Strength: 5 mg and 10 mg</p> <p>Dosage form: tablet</p> <p>Dose: 5 mg to 10 mg once daily</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xa” vs. “Le”. The letters “temis” may appear similar to the letters “tairis” when scripted</p> <p>Both names have similar shape and length.</p> <p>Phonetic similarities:</p> <p>Both names contain suffices that contain two syllables with the suffix “is” and may sound similar “temis” vs. “tairis”</p> <p>Overlapping Product Characteristics:</p> <p>Route of administration: oral</p>	<p>Orthographic Differences:</p> <p>Xartemis prefix contains the letter “r” before the upstroke letter “t” elongating the Xartemis prefix vs. Letairis</p> <p>Phonetic differences:</p> <p>The prefix “Xar” with the “Z” sound and the “ar” sound does not sound similar to the prefix “Let” with “L” sound and the short “e” sound</p> <p>Product Characteristic Differences:</p> <p>Strength: Xartemis has a single strength which may be omitted from the prescription vs. Letairis has two strengths which must be included. There are no overlapping strengths.</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Letairis is once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Lotemax (loteprednol etabonate)</p> <p>Strength: 0.5%</p> <p>Dosage form: ophthalmic suspension, ointment and gel</p> <p>Dose: suspension: 1 to 2 drops into the conjunctival sac 4 times a day, may increase up to 1 drop every hour during the first week; gel and suspension: 1 to 2 drops into the conjunctival sac 4 times daily starting the day after surgery and continuing for 2 weeks; ointment: apply approximately one-half inch ribbon into the conjunctival sac 4 times daily starting 24 hour after surgery and continuing for 2 weeks</p> <p>Route of Administration: ophthalmic</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xa” vs. “Lo”. The letters “temis” may appear similar to the letters “temax” when scripted</p> <p>Both names have similar shape and length.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both names have a single strength which may be omitted from the prescription</p> <p>Dose: Xartemis is expressed as “2 tablets” and Lotemax may be expressed as “2 drops”</p>	<p>Orthographic Differences:</p> <p>Xartemis prefix contains the letter “r” before the upstroke letter “t” elongating the Xartemis prefix vs. Lotemax</p> <p>Product Characteristic Differences:</p> <p>Form: Xartemis has a single dosage form which may be omitted vs. Lotemax has multiple dosage forms which must be included</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Lotemax is four times daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Ventavis (Iloprost)</p> <p>Strength: 10 mcg/mL and 20 mcg/mL</p> <p>Dosage form: nebulizer inhalation solution in 1 mL glass container</p> <p>Dose: initial, 2.5 mcg using the I-neb ADD System or the Prodose AAD System. If tolerated, increase dose to 5 mcg every 2 - 4 hours or 6 to 9 times per day (no more than every 2 hours) during waking hours; maximum daily dose 45 mcg (5 mcg 9 times per day)</p> <p>Route of Administration: inhalation</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xar” vs. “Ven”. The infix and suffix letters “temis” may appear similar to the letters “tavis” when scripted</p> <p>Both names have similar shape and length.</p>	<p>Product Characteristic Differences:</p> <p>Strength: Xartemis has a single strength which may be omitted from the prescription vs. Ventavis has two strengths which must be included. There are no overlapping strengths.</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Ventavis is every 2 to 4 hours or 6 to 9 times per day</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xalatan (latanoprost)</p> <p>Strength: 0.005%</p> <p>Dosage form: ophthalmic solution drops supplied as a 2.5 mL solution in a 5 mL bottle with a dropper tip</p> <p>Dose: one drop in the affected eye(s) once daily in the evening (Not to exceed once daily)</p> <p>Route of Administration: ophthalmic</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes “Xa”.</p> <p>Both names have similar length.</p> <p>Phonetic similarities:</p> <p>Both names begin with prefixes “Xa”.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both names have a single strength which may be omitted from the prescription</p>	<p>Orthographic Differences:</p> <p>The infix and suffix letters “rtemis” are not similar to the letters “latan” when scripted</p> <p>Phonetic differences:</p> <p>The infixes and suffices “temis” and “latan” do not sound similar</p> <p>Product Characteristic Differences:</p> <p>Dose: Xartemis is expressed as “2 tablets” and Xalatan may be expressed as “one drop”</p> <p>Frequency:</p> <p>Xartemis is every 12 hours vs. Xalatan is once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xalkori (crizotinib)</p> <p>Strength: 200 mg and 250 mg</p> <p>Dosage form: capsule</p> <p>Dose: 250 mg twice daily or 200 mg twice daily or 250 mg once daily</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes “Xa”.</p> <p>Both names have similar length.</p> <p>Overlapping Product Characteristics:</p> <p>Frequency: every 12 hours vs. twice daily</p> <p>Route of administration: oral</p>	<p>Orthographic Differences:</p> <p>The infix and suffix letters “rtemis” are not similar to the letters “lkori” when scripted</p> <p>Product Characteristic Differences:</p> <p>Strength: Xartemis has a single strength which may be omitted from the prescription vs. Xalkori has two strengths which must be included. There are no overlapping strengths.</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xarelto (rivaroxaban)</p> <p>Strength: 10mg, 15mg, 20mg</p> <p>Dosage form: tablet</p> <p>Dose: 15 mg twice daily, 15 mg once daily, 10 mg once daily, 20 mg once daily; CrCl > 50 mL/min: 20 mg once daily; CrCl 15 to 50 mL/min, 15 mg once daily; CrCl less than 15 mL/min; avoid use</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity: Both names begin with prefixes “Xar”. Both names have similar length.</p> <p>Phonetic similarities: Both names begin with prefixes “Xar”.</p> <p>Overlapping Product Characteristics: Frequency: every 12 hours vs. twice daily Route of administration: oral</p>	<p>Orthographic Differences: The infix and suffix letters “temis” are not similar to the letters “elto” when scripted, due to the different placement of the upstroke letters</p> <p>Phonetic differences: The infixes and suffices “temis” do not sound similar to “elto”</p> <p>Product Characteristic Differences: Strength: Xartemis has a single strength which may be omitted from the prescription vs. Xarelto has multiple strengths which must be included. There are no overlapping strengths.</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xenaderm (Balsam peru/Castor/trypsin) Wound healing, Pressure ulcers, varicose ulcers, dehiscent wounds</p> <p>Strength: 788 mg/87 mg/90 units</p> <p>Dosage form: ointment</p> <p>Dose: apply a thin film to the wound area at least twice daily or as frequently as needed</p> <p>Route of Administration: topical</p>	<p>Orthographic similarity: Both names begin with prefixes that may appear similar when scripted “Xar” vs.” Xen”. Both names have similar length.</p> <p>Overlapping Product Characteristics: Strength: Both names have single strength which may be omitted from the prescription Frequency: every 12 hours vs. twice daily</p>	<p>Orthographic Differences: The infix and suffix letters “temis” are not similar to the letters “aderm” when scripted, due to the different placement of the upstroke letters</p> <p>Product Characteristic Differences: Dose: Xartemis is expressed as “2 tablets” and Xenaderm may be expressed as “apply”</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xiaflex (Collagenase clostridium histolyticum)</p> <p>Dupuytren’s contracture with a palpable cord</p> <p>Strength: 0.9 mg</p> <p>Dosage form: intralesional injection solution</p> <p>Dose: Inject 0.58 mg into a palpable Dupuytren’s cord with a contracture of a metacarpophalangeal joint or a proximal interphalangeal joint according to the injection procedure. Injections and finger extension procedures may be administered up to 3 times per cord at approximately 4-week intervals.</p> <p>Route of Administration: intralesional</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xarte” vs.” Xiafl”.</p> <p>Both names have similar length.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both names have single strength which may be omitted from the prescription</p>	<p>Orthographic Differences:</p> <p>The suffix letters “mis” are not similar when scripted to the suffix “ex”.</p> <p>Product Characteristic Differences:</p> <p>Dose: Xartemis is expressed as “2 tablets” and Xiaflex may be expressed as “inject”</p> <p>Frequency: Xartemis is every 12 hours vs. Xiaflex monthly</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xtramins (multiple vitamin)</p> <p>Strength: N/A</p> <p>Dosage form: tablet</p> <p>Dose: one tablet once daily</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with letter “X” and contain a suffix that may appear similar when scripted “mis” vs. “min”. Both names have similar length.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both names have single strength which may be omitted from the prescription</p> <p>Route of administration: oral</p>	<p>Orthographic Differences:</p> <p>The prefix and infix “Xarte” is not orthographically similar to the prefix “Xtra” due to the different placement of the upstroke letter ‘T’.</p> <p>Product Characteristic Differences:</p> <p>Frequency: Xartemis is every 12 hours vs. Xtramins once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Xuriden (uridine triacetate) antidote to excess 5-FU or therapeutic enhancement of 5-FU activity</p> <p>Strength: 6 gram and 10 gram</p> <p>Dosage form: oral granules</p> <p>Dose: Antidote: 10 grams every 6 hours for a total of 20 doses Therapeutic: 6 grams every 8 hours for a total of 8 doses following each dose of high dose 5-fluorouracil</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity: Both names begin with prefixes that may appear similar when scripted “Xar” vs.” Xur”.</p> <p>Both names have similar length.</p> <p>Overlapping Product Characteristics: Route of administration: oral</p>	<p>Orthographic Differences: The infix and suffix “temis” is not similar to the infix and suffix “iden” when scripted due to the different placement of upstroke letters</p> <p>Product Characteristic Differences: Dose: Xartemis is expressed as “2 tablets” and Xuriden may be expressed as “grams”</p> <p>Strength: Xartemis has a single strength which may be omitted from the prescription vs. Xuriden has multiple strengths which must be included. There are no overlapping strengths.</p> <p>Frequency: Xartemis is every 12 hours vs. Xuriden every 6 or 8 hours</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Zarontin (ethosuximide) absence seizures</p> <p>Strength: 250 mg and 250 mg/mL</p> <p>Dosage form: capsule or syrup</p> <p>Dose: 3 to 6 years of age is 250 mg once daily; 6+ years of age 500 mg once daily</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity: Both names begin with letters that may appear similar when scripted “X” vs. “Z”, when the letter Z is written with a crosstroke. Both contain the letters “ar” in the prefix</p> <p>Phonetic similarities: Both names begin with prefixes that may sound similar “Xar” vs. “Zar”</p> <p>Overlapping Product Characteristics: Route of administration: oral</p>	<p>Orthographic Differences: The infixes and suffices are not similar when scripted, “temis” vs. “ontin” due to the different placement of the upstroke letter “T”</p> <p>Phonetic differences: The infixes and suffices do not sound similar “temis” vs. “ontin”</p> <p>Product Characteristic Differences: Strength: Xartemis has a single strength which may be omitted from the prescription vs. Zarontin has multiple strengths which must be included. There are no overlapping strengths.</p> <p>Dosage form: Xartemis has a single dosage form which may be omitted vs. Zarontin has two dosage forms which must be specified on the prescription</p> <p>Frequency: Xartemis is every 12 hours vs. Zarontin once daily</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Zofran (ondansetron hydrochloride) Strength: 2 mg/mL and 4 mg/5 mL and 24 mg, 4 mg , and 8 mg</p> <p>Dosage form: injectable injection, tablet, orally disintegrating tablet, oral solution</p> <p>Dose: Adults intravenous: 0.15 mg/kg (70 kg =10.5 mg) infused over 15 minutes 30 minutes prior to emetogenic chemotherapy. No single dose should exceed 16 mg/dose IV repeated twice, at 4 and 8 hours after the initial dose Infants >= 6 months, children and adolescents intravenous: 0.15 mg/kg IV (45 kg = 6.75 mg) infused over 15 minutes 30 minutes prior to chemotherapy and repeat 4 and 8 hours later (3 doses total). Maximum: 16 mg/dose; Oral Adults: 8 mg twice daily or single 24 mg dose 30 minutes prior to highly emetogenic chemotherapy or 8 mg three times daily or 8 mg 1—2 hours prior to each fraction of radiotherapy each day or 8 mg every 8 hours Oral Children and Adolescents >= 12 years: 8 mg twice daily and then 16 mg every 8 hours for 1—5 days or as a single 24 mg dose</p>	<p>Orthographic similarity: Both names begin with prefixes that may appear similar when scripted “Xa” vs. “Zo”, when the letter “Z” is written with a cross stroke. The infix letters “te” may appear similar when scripted vs. “fr”</p> <p>Phonetic similarities: Both names begin with prefixes that may sound similar “Xar” vs. “Zo”</p> <p>Overlapping Product Characteristics: Frequency: Xartemis is every 12 hours vs. Zofran twice daily Route of administration: oral</p>	<p>Orthographic Differences: The letter “r” in the “Xar” elongates the name vs. “Zo”. The suffix “mis” is not orthographically similar to the suffix “on” and elongates the name vs. Zofran.</p> <p>Phonetic differences: The infixes and suffix “temis”, which has two syllables, does not sound similar to “fran”, which has one syllable</p> <p>Product Characteristic Differences: Strength: Xartemis has a single strength which may be omitted from the prescription vs. Zofran has multiple strengths which must be included. Dosage form: Xartemis has a single dosage form which may be omitted vs. Zofran has three dosage forms which must be specified on the prescription</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Zostavax (herpes Zoster Virus vaccine)</p> <p>Strength: 19400 PFU</p> <p>Dosage form: powder for solution</p> <p>Dose: Adults aged 50 years +: 0.65 mL once</p> <p>Route of Administration: subcutaneous</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xar” vs. “Zos”. The infixes and suffices may appear similar when scripted “temis” vs. “tavax”</p> <p>Both names have similar shape and length.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: Both names have single strength which may be omitted from the prescription</p>	<p>Product Characteristic Differences:</p> <p>Dose: Xartemis is expressed as “2 tablets” and Zostavax is expressed in “mL”</p> <p>Frequency: Xartemis is every 12 hours vs. Zostavax once</p>

<p>Xartemis (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Zostrix (capsaicin) pain associated with osteoarthritis and rheumatoid arthritis, psoriasis</p> <p>Strength: 0.025%, 0.075%</p> <p>Dosage form: emollient cream or topical stick</p> <p>Dose: apply thin film to the affected area 3 to 4 times daily or 6 times daily for three days then 4 times daily</p> <p>Route of Administration: topical</p>	<p>Orthographic similarity: Both names begin with prefixes that may appear similar when scripted “Xar” vs. “Zos”.</p> <p>Phonetic similarities: Both names begin with prefixes that may sound similar “Xar” vs. “Zo”</p>	<p>Orthographic Differences: The infix and suffix “temis”, appearing orthographically elongated, is not similar to the suffix “trix”.</p> <p>Phonetic differences: The infix and suffix “temis”, which has two syllables, does not sound similar to the suffix “trix”, which has one syllable.</p> <p>Product Characteristic Differences: Strength: Xartemis has a single strength which may be omitted from the prescription vs. Zostrix has multiple strengths which must be included.</p> <p>Dose: Xartemis is expressed as “2 tablets” vs. Zostrix may be expressed as “apply”</p> <p>Dosage form: Xartemis has a single dosage form which may be omitted vs. Zostrix has two dosage forms which must be specified on the prescription</p>

Appendix E.2: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Xartemis XR (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
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(b) (4)

<p>Xartemis XR (oxycodone hydrochloride and acetaminophen) Controlled Release Tablets</p> <p>Dosage Form: tablets</p> <p>Strength(s): 7.5 mg/325 mg</p> <p>Usual Dose: two tablets every 12 hours</p> <p>Route of Administration: oral</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names</p>
<p>Zortress (everolimus) prophylaxis of organ rejection in adults</p> <p>Strength: 0.25 mg, 0.5 mg, 0.75 mg</p> <p>Dosage form: tablet</p> <p>Dose: 0.75 mg twice daily (kidney txp); 1 mg twice daily (liver txp). Adjust maintenance dose to achieve everolimus trough concentrations within the 3-8 ng/mL</p> <p>Route of Administration: oral</p>	<p>Orthographic similarity:</p> <p>Both names begin with prefixes that may appear similar when scripted “Xart” vs. “Zort”.</p> <p>Both names have similar shape.</p> <p>Overlapping Product Characteristics:</p> <p>Strength: 7.5 mg vs. 0.75 mg</p> <p>Frequency: every twelve hours vs. twice daily</p> <p>Route: oral</p>	<p>Orthographic Differences:</p> <p>The infix/suffix “emis” is not orthographically similar to the infix/suffix “ress” as the letter “m” in Xartemis XR confers elongation</p>

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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