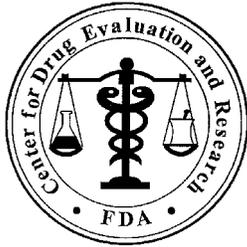


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-233

PROPRIETARY NAME REVIEW(S)



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

Date: August 6, 2008

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Subject: Proprietary Name Review for Aloxi

Drug Name(s): Aloxi (Palonosetron HCl) capsules

Application Type/Number: NDA # 22-233

Applicant: Helsinn Healthcare

OSE RCM #: 2007-2522

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EXECUTIVE SUMMARY

The Division of Medication Error Prevention and Analysis does not object to the proposed proprietary name, Aloxi, although our Proprietary Name Risk Assessment findings indicate that the name is vulnerable to name confusion that could lead to medication errors. Specifically, we identified potential name confusion with the existing products, Adoxa, Alora and Olux-E. Although this finding would typically lead the DMEPA to object to the proposed proprietary name, FMEA of alternatives approaches to address this name confusion, including a new name for palonosetron capsules, a new name for all palonosetron HCL products, or use of a modifier with the name, also found potential opportunities for medication errors. As the FMEA noted some detectability of the medication errors resulting from name confusion, we will not object to the use of the name, Aloxi, for this product. However, we provide recommendations to the Applicant in Section 5.2.1 to monitor medication errors related to Aloxi and report these errors to the Agency regardless of the severity of the adverse events.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from the Division of Gastroenterology (HFD-180), for the assessment of the proprietary name, “Aloxi,” for the product, NDA 22-233, regarding its potential confusion with other proprietary or established drug names in normal practice settings resulting in medication errors.

1.2 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis previously reviewed the proprietary name, Aloxi, for IND # 39,797, palonosetron HCl injection in OSE Review # 02-0068, dated July 16, 2002 and objected to the use of the name based on its orthographic similarity to Alora including similarity of strength and dose. However, upon the Applicant’s change in the dose of Aloxi to 0.25 mg, our Division found the name Aloxi acceptable in OSE review # 02-0068-2, dated March 18, 2003. Aloxi (palonosetron HCl) injection was approved as NDA # 21-372 by the Agency on July 25, 2003.

1.3 PRODUCT INFORMATION

Aloxi (palonosetron HCl) capsules is a serotonin 5-HT₃ antagonist indicated the prevention of acute (b) (4) nausea and vomiting associated with moderately emetogenic chemotherapy. The 0.5 mg capsule represents a new dosage form, new strength, and new route of administration for palonosetron HCl. One capsule is taken orally one hour prior to the start of chemotherapy without regard to food. Aloxi is packaged in bottles containing five capsules and is stored at room temperature.

2 METHODS AND MATERIALS

FDA’s Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Aloxi, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Aloxi, the medication error prevention staff searches a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.2). Our Division also conducts internal CDER prescription analysis studies (see 2.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment. In addition, as Aloxi is the name of a currently marketed product, the Division of Medication Error Prevention and Analysis includes a search of the Adverse Events Reporting System (AERS) database as part of the Proprietary Name Risk Assessment to identify cases of name confusion or other potential sources of medication errors with the product.

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 (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.¹ FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The medication error prevention staff 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 Our staff uses our clinical expertise to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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, the medication error prevention staff considers the potential for confusion throughout the entire

¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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

U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

2.1 SEARCH CRITERIA

The medication error prevention staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘A’ 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.⁴⁵

To identify drug names that may look similar to Aloxi, the staff also considers the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (five letters), upstrokes (two, capital letter ‘A’ and lower case ‘l’), downstrokes (none), cross-strokes (one, lower case ‘x’), and dotted letters (one, lower case ‘i’). Additionally, several letters in Aloxi may be vulnerable to ambiguity when scripted, including the letter ‘A’ may appear as ‘Ce,’ ‘Ci,’ ‘Cl,’ or ‘O’; lower case ‘l’ may appear as a lower case ‘b,’ ‘d’ or ‘e’; ‘-ox-’ may appear as ‘-en’; ‘x’ may appear as ‘f,’ ‘n,’ ‘p’ ‘r,’ or ‘t’; and ‘i’ may appear as ‘e’. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Aloxi.

When searching to identify potential names that may sound similar to Aloxi, the medication error prevention staff searches for names with similar number of syllables (three), stresses (ah-LOCKS-ee or AH-locks-EE), and placement of vowel and consonant sounds. In addition, several letters in Aloxi may be subject to interpretation when spoken, including the letter ‘x’ which may be interpreted as ‘cks’ or ‘z’ and ‘i’ which may be misinterpreted as ‘e’ or ‘y.’ As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Aloxi.

The staff also considers the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the medication error prevention staff were provided with the following information about the proposed product: the proposed proprietary name (Aloxi), the established name (palonosetron HCl), proposed indication (prevention of acute (b) (4) nausea and vomiting associated with moderately emetogenic chemotherapy), strength (0.5 mg), dose (0.5 mg or one capsule), frequency of administration (one hour before start of chemotherapy), route (oral) and dosage form of the product (capsule). Appendix A provides a more detailed listing of the product characteristics the Staff generally takes into consideration.

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

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Lastly, the medication error prevention staff also considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error prevention staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1 Database and Information Sources

The proposed proprietary name, Aloxi, was provided to the medication error prevention staff to conduct a search 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 Aloxi using the criteria outlined in 2.1. A standard description of the databases used in the searches is provided in Section 6.2. To complement the process, the medication error staff 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, the medication error prevention staff reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the medication error prevention staff to gather CDER professional opinions on the safety of the product and the proprietary name, Aloxi. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the medication error prevention staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

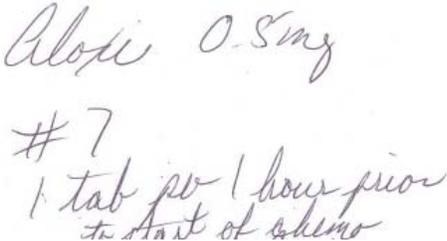
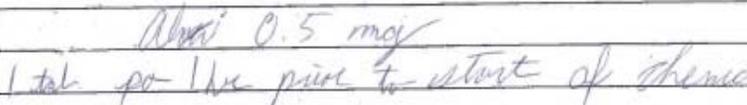
2.2 CDER PRESCRIPTION ANALYSIS STUDIES

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Aloxi 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 a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

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

proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 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 the medication error staff.

Figure 1. Aloxi Prescription Study (conducted on January 18, 2008)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> 	<p>Aloxi 0.5 mg #7 Take one tablet by mouth one hour prior to start of chemotherapy.</p>
<p><u>Inpatient Medication Order:</u></p> 	

2.3 ADVERSE EVENTS REPORTING SYSTEM (AERS) DATABASE

Because Aloxi has been marketed since 2003, the medication error prevention staff conducted a search of the Adverse Events Reporting System (AERS) database to determine if medication errors related to name confusion have been reported. The staff searched the database using the following criteria: the High Level Group Term (HLGT) “Medication Errors” and Preferred Term (PT) “Pharmaceutical Product Complaint, the Active Ingredients “palonosetron,” the Trade name, “Aloxi,” and the Verbatim Substance Name “Alox%.”

The cases were manually reviewed to determine if a medication error occurred. If an error occurred, the staff reviewed the case to determine if the root cause could be associated with the nomenclature of the product, and thus pertinent to this review. Those cases that did not describe a medication error or did not describe an error applicable to this review were excluded from further analysis. The cases that did describe a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors.

2.4 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, the medication error prevention staff seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike 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 not yet marketed, the safety evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking: “Is the name Aloxi 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 Aloxi 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 and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

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

The Division of Medication Error Prevention and Analysis will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The medication error prevention staff 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. The medication error prevention staff identifies a potential source of medication error within the proposed proprietary name. 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.

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

If none of these conditions are met, then the medication error prevention staff will not object to the use of the proprietary name. If any of these conditions are met, then our division will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, the World Health Organization, the Joint Commission, and the Institute for Safe Medication Practices, that have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the medication error prevention staff 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, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name

changes, have been undertaken 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 the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the medication error prevention staff 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 limitations of the process).

If the medication error prevention staff objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. Our Division is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for the medication error prevention staff to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

Our search yielded seven names as having some similarity to the name Aloxi.

Five of the seven names that were thought to look like Aloxi, which include: Adoxa, Avelox, Alora, Aleve, and Ciloxan. One name, Olux-E, was thought to sound similar to Aloxi. The remaining name, Alli, was thought to look and sound similar to Aloxi.

A search of the United States Adopted Name stem list on April 17, 2008, identified no USAN stems within the proposed name, Aloxi.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by the medication error prevention staff (see section 3.1.1. above), and noted no additional names thought to have orthographic similarity to Aloxi and have the potential for confusion. The name Ciloxan, was misspelled as Ciloxin when presented to the Expert Panel. However, the primary Safety Evaluator considered the correct spelling in the Risk Assessment (section 3.1.5).

Ten names from OSE review # 02-0068 were presented to the Expert Panel as the product characteristics for Aloxi have changed in this NDA. One of the ten previously considered names, (b) (4), was thought to sound similar to Aloxi. The remaining nine names, Alesse, Alocril (misspelled as Alocrit at Expert Panel), Alomide, Amoxil, Floxin, Lanoxin, M-Oxy, and Roxicet were thought to look and sound similar to Aloxi.

DDMAC had no concerns regarding the proposed name from a promotional perspective and noted Aloxi is the name of a currently marketed product.

3.3 CDER PRESCRIPTION ANALYSIS STUDIES

A total of 35 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. More than 70% of the participants (n=25) interpreted the name correctly as “Aloxi,” with correct interpretation occurring more frequently in the outpatient written study. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the written inpatient prescription study, with the ‘-oxi’ in Aloxi misinterpreted by one respondent each as ‘-aw,’ ‘-otri,’ ‘ori,’ and ‘oi’ and by two respondents each as ‘-va’ and ‘-avi’ . In the verbal prescription, the ending letter ‘i’ was misinterpreted as a ‘y’ by two respondents. See Appendix A for the complete listing of interpretations from the verbal and written prescription studies.

3.4 ADVERSE EVENTS REPORTING SYSTEM DATABASE (AERS)

The search yielded one case (n=1) of a dosing error which resulted in the administration of an extra dose of Aloxi. Our review of the case noted no contributing factors related to the name, Aloxi, or the product label or labeling.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified an additional ten names thought to look and/or sound similar to Aloxi and represent a potential source of drug name confusion. Seven of the ten names were thought to look similar to Aloxi including: Abreva, Alax, Cedax, Celexa, Celontin, Celox, and Cidex. Two of the ten names, Aloxyn and Eloxatin, were thought to sound similar to Aloxi. The remaining name, Alaxa, was thought to look and sound similar to Aloxi. As such, a total of 27 names were analyzed to determine if the drug names could be confused with Aloxi and if the drug name confusion would likely result in a medication error.

Five of the 27 identified names were determined to lack sufficient orthographic and/or phonetic similarity to Aloxi to present a risk of confusion. These names include: Avelox, Droxy, Lanoxin, M-oxy and Roxicet® (See Appendix C).

The remaining 22 identified names were determined to have some orthographic and/or phonetic similarity to Aloxi, and thus determined to present some risk of confusion. Failure mode and effect analysis was then applied to determine if the potential name, Aloxi, could potentially be confused with any of these 22 names and lead to medication errors.

This analysis determined that the name similarity between Aloxi and the identified names was unlikely to result in medication errors for 19 product names. Three of the 19 products (Alax, Alaxa and Aloxyn) are only marketed in foreign countries (see Appendix D). Although used in healthcare settings, two products (Celox and Cidex) are not medications and are not likely to be confused with medications in normal practice settings. (See Appendix E.)

For eight of the 19 names (Abreva, Alocril, Alomide, Cedax, Celexa, Celontin, Ciloxan, and Floxin), FMEA determined that medication errors were unlikely due to minimal orthographic and/or phonetic similarity to Aloxi as well as they do not overlap in strength or dose with Aloxi (Appendix F).

The three of the 19 names (Aloprim, Amoxil and Eloxatin) have some numerical strength overlap with Aloxi. In addition, three names (Aleve, Alesse, and Alli) are, like Aloxi capsules, available only in one strength leading to the omission of the strength in a prescription or

requisition for the product. However, analysis of the failure mode of these six product names did not determine the effect of these similarities to result in medication errors in the usual practice setting (Appendix G).

The remaining product names, Adoxa, Alora, and Olux-E, were determined to be potential source of medication error. The products share numerical overlap in strength and are likely to have directions for use written as ‘Use as directed.’ (See Appendix H)

If Aloxi was not approved for this application, it would result in the use of a different proprietary name for the oral formulation of palonosetron HCL. This introduces a dual trade name creating other opportunities for medication errors. Additionally, the alternative of using a modifier with the proposed name, Aloxi, for the oral formulation product may also introduce opportunity for error. Therefore, the safety evaluator completed a Failure Mode and Effects Analysis for each nomenclature option including detectability of the error and regulatory means for managing the risks of the error. (See Appendix H).

4 DISCUSSION

The Proprietary Name Risk Assessment found that confusion between Aloxi and Adoxa, Alora, or Olux-E has the potential to result in a medication error because of the new dosage form and strength. Prior reviews of the name Aloxi by this Division evaluated the product as an injection which limited the usual practice setting primarily to outpatient clinics and inpatient areas. The new Aloxi dosage form of a 0.5 mg capsule changes several of the associated product characteristics such as route of administration, how directions for use may be written, and the practice settings. As this proposed product may be more likely used in the outpatient setting than the injection formulation, it introduces new opportunities for error. All of the products names identified as a safety concern in this review are primarily used in outpatient practice settings. This provides opportunity for prescriptions for Aloxi to be introduced in this environment where they would not previously existed. This new overlap does not provide an environment where these products can co-exist without the potential for confusion.

4.1 NAME CONFUSION

The following product names are vulnerable to confusion with Aloxi because of the new dosage form, route of administration, strength, and setting of use.

4.1.1 Adoxa and Aloxi

The orthographic similarities between Aloxi and Adoxa stem from the fact that both names begin with the letter ‘A’ and share an ‘o’ and ‘x’ in the third and fourth positions, respectively. In addition, the second letter in each name provides an upstroke (‘l’ in Aloxi compared to the ‘d’ in Adoxa). The samples provided below demonstrate the similarity between these products.



The image shows six handwritten samples of the words 'Adoxa' and 'Aloxi' in cursive. The first sample is 'Adoxa', the second is 'Aloxi', the third is 'Aloxi' with a horizontal line above it, the fourth is 'Adoxa', the fifth is 'Aloxi', and the sixth is 'Adoxa'. The handwriting is consistent across all samples, illustrating the orthographic similarities between the two names.

In the initial review of the proposed name, Aloxi (OSE review # 02-0068), the safety evaluator identified the name, Adoxa, as likely to be confused with Aloxi. However, the safety evaluator noted the route of administration, dosage form, and dosing regimens as differences that would prevent these products from being confused. The products now share route of administration as

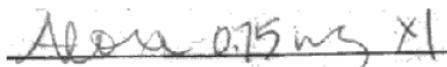
these products are both oral solid dosage forms. In addition, although the directions for use may differ between these products, we believe it is likely prescribers will write, ‘Use as directed.’ after explaining the proper use of the medication rather than writing the complete and lengthy directions for use on a prescription. These products also share numerically similar strengths (0.5 mg and 50 mg). In addition, the Applicant expresses the strength of Aloxi capsules as 0.50 mg with a trailing zero as noted in the submitted draft package insert labeling which may provide the opportunity for readers to incorrectly see “50 mg” in the 0.50 mg strength.

The FMEA included the ability to detect the error related to the confusion of these two names prior to the patient consuming the product. The ability to detect a medication error resulting from this confusion is hindered by the fact the patient would receive either product as an oral dosage form. However, if the patient receives patient counseling from the pharmacist at the time of dispensing and discusses the indication of use, the medication error may be identified. The quantity to dispense for Adoxa is likely to be higher when compared to Aloxi as Adoxa is an antibiotic, doxycycline, which is usually administered every six hours on the first day, followed by twice a day for a total of seven to ten days of therapy (i.e. 16 to 22 tablets). The quantity to dispense for Aloxi will likely be based on the number of consecutive days of chemotherapy treatment (i.e. one to five doses).

4.1.2 Alora and Aloxi

The look-alike similarity between Alora and Aloxi stems from the fact that both names begin with the same three letters, ‘Alo-.’ Both names contain five letters and thus have the same length. In addition, ten responses to the prescription study for Aloxi completed for OSE Review 03-0068 were Alora. The sample from aforementioned review (Figure 2 on page 13) demonstrates the ‘xi’ in Aloxi can appear as ‘ra.’ This similarity resulted in the Safety Evaluator conclusion that Aloxi would be confused with Alora.

Figure 2: Inpatient sample of OSE Review # 03-0068



A handwritten sample of a prescription for Aloxi. The word 'Aloxi' is written in cursive as 'Alora'. To the right of 'Alora' is '0.75mg' and further right is 'x1'. The entire text is underlined.

Several products characteristics of Aloxi and Alora overlap including; a numerically similar strength (0.5 mg vs. 0.05 mg), directions for use are likely to be written as ‘Use as directed,’ and dispensed from outpatient pharmacies. In addition, the quantities in which these products are packaged (five capsules of Aloxi vs. eight patches of Alora) appear similar when written. The quantity to dispense for Alora may be written in terms of month’s supply. Therefore, we believe a potentially low dispensing quantity for Aloxi is likely to be misinterpreted by pharmacy staff as the number of months to provide. We note the safety evaluator who previously reviewed the name Aloxi rescinded his objection to the name based on the removal of the 0.75 mg/15 mL strength of Aloxi. However, we note that the safety evaluator for Aloxi in OSE review # 03-0068 and #03-0068-2 failed to note that Alora was and is available in 0.025 mg strength.

The FMEA notes the confusion between these products has a moderate level of detectability based on the fact Alora is an external use transdermal system while Aloxi will be taken orally. If an error results from the confusion of these names, a patient familiar with the Aloxi dosage form may be able to identify the wrong medication was dispensed by the fact the dosage form and route of administration differ from what was expected.

4.1.3 *Olux-E and Aloxi*

The sound alike similarity between Olux-E and Aloxi stems from the facts that both names contain three syllables, begin with similar sounding vowel sounds ('Oh-' in Olux-E vs. 'Ah-' in Aloxi), and the second and third syllables sound nearly the same when spoken ('luks-ee' in Olux-E vs. 'locks-ee' in Aloxi).

Olux-E and Aloxi differ in many product characteristics such as dosage form (topical foam vs. capsule), route of administration (topical vs. oral), frequency of administration (twice daily vs. one hour prior to chemotherapy, prescribing population (dermatologists vs. oncologist), and patient populations. However, the products do share some key overlapping characteristics which may be included in a written patient prescription including: numerically similar strengths (0.05% vs. 0.5 mg), directions for use may be written with 'Use as directed', dispensed from outpatient pharmacies, and a low number for a dispensing quantity (one or two). Olux-E is only available in one size container (100 g). Therefore, the can size for Olux-E may be omitted when a prescription is called to a pharmacy eliminating this potential differentiating characteristic. When these products were compared previously in OSE review # 2006-1128, the reviewing safety evaluator noted the limited practice setting for Aloxi of hospital and clinic settings minimizing the potential for medication errors as dose and actual frequency are required by the Joint Commission in these settings. The proposed product's dosage formulation eliminates the practice setting difference.

The FMEA notes the confusion between these products has a moderate level of detectability based on the fact Olux-E is a topical foam used externally while Aloxi will be taken orally. If an error results from the confusion of these names, the patient may be able to identify the wrong medication was dispensed by the fact the dosage form and route of administration differ from what was expected.

4.2 ALTERNATIVE NAMES

The third reason noted in Section 2.4 to object to a proposed proprietary name states, "FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice." Since Aloxi would now likely be confused with existing proprietary names because of the new strength, dosage form, route of administration and setting of use, we would have found the name unacceptable and thus, would have to approve the product under a new name. However, the introduction of an alternative name for either the palonosetron HCl capsules or all the palonosetron HCl products potentially creates opportunities for medication errors as well. As such, we considered three options for alternative names in our assessment, the use of a new name for just the capsule formulation, an alternative name for all palonosetron HCl products, and use of a modifier for the capsule formulation. Our assessment identifies regulatory methods to manage the risk of medication error for each alternative.

4.2.1 *Alternative name for capsules*

The introduction of an alternative proprietary name for the oral formulation of palonosetron HCl may address the concern of potential confusion in the outpatient setting. However, the FMEA of this approach notes the potential for duplicate therapy medication errors resulting in a palonosetron HCl overdose. The medication error prevention staff's post-marketing surveillance

of medication errors reveals that overdoses of medication occur when a prescriber, unfamiliar with all proprietary names of a medication, prescribes a medication to the patient who is already receiving the same medication under a different proprietary name. In addition, the use of dual trade names has been implicated in a medication error case report as a cause of overdosing patients.⁷

Additionally, administration of the same medication by two different routes is a concern in the inpatient or hospital setting. Research in this setting has demonstrated that prescribing the same or similar medication to be given concurrently by two routes of administration to be a common source of medication error.⁸ The same study indicated the prescribing of the same or similar medication to be given concurrently via the intravenous and oral route of administration as the most common type of prescribing error. We believe this duplicate therapy type of medication error would more likely result if an alternative proprietary name for the oral formulation was implemented. This error may have a low detectability as healthcare providers in the hospital setting are more familiar with Aloxi as the proprietary name for palonosetron HCl and thus may not recognize the alternative name, especially at the launch of the new dosage form.

The FMEA identified methods to manage this risk of duplicate therapy, which include: allowing Aloxi for the oral formulation which is likely to result in the name confusion medication errors discussed in Section 4.1.1, choosing an alternative name for the oral and injectable formulations of palonosetron HCl (See Section 4.2.2 below), or adding modifier to the name, Aloxi, for the oral capsule, (See Section 4.3).

4.2.2 Alternative name for all palonosetron HCl products

Another identified method to reduce the potential for name confusion would be recommending the use of an alternative proprietary name for all of the palonosetron HCl products, including those already marketed. This approach provides all the palonosetron products with one proprietary name, which eliminates the opportunity of potential medication errors associated with dual trade names, such as duplicate therapy.

However, post-marketing surveillance demonstrates that prescribers continue to use proprietary names they have become familiar with even after the name or the product has been removed from the marketplace. (e.g. “Serzone” for nefazodone or “Reminyl” for Razadyne). Thus, the continued use of an error-prone trade name causes medication errors to continue. In addition, we believe inpatient pharmacies and drug wholesalers are likely to have some quantities of Aloxi injection available on the shelf at the time of release of any alternatively named product adding to dual trade name errors as both Aloxi and alternatively named palonosetron products may simultaneously be available.

Historically, the Agency requests names changes for marketed products after documented errors have occurred. The FMEA demonstrates the potential for the proposed name, Aloxi, to be confused with existing products based on the new product characteristics. Our search of the AERS database identified no cases of name confusion with Aloxi. Additionally, our analysis

⁷ Schwab, M, et. al., Using Trade Names : A Risk Factor for Accidental Drug Overdose, Arch Intern Med. 2002; 162: 1065-1066.

⁸ Lesar TS. Medication Prescribing Errors Involving Route of Administration. Hosp Pharmacy. 2006; 41(11): 1053-1066.

also demonstrates that the likelihood of the error to be detected is low due to fact inpatient healthcare providers are likely to be more familiar with the currently marketed product name, Aloxi, at the time a proposed alternative name would be launched.

The FMEA identified methods to manage this risk of duplicate therapy, which include: allowing Aloxi for the oral formulation which is likely to result in the name confusion medication errors discussed in Section 4.1.1 or adding modifier to the name, Aloxi, for the oral capsule.

4.3 USE OF A MODIFIER

Another regulatory option identified for differentiating product names would be to add a modifier (i.e., prefix or suffix) to the proposed name, Aloxi, to better distinguish it from names identified as potentially confusing. In this case, the modifier would be added to the capsule formulation. The FMEA identified two possible failure modes with the use of modifiers we have noted in post-marketing surveillance as contributing factors to medication errors. (See Appendix H.)

When a product name includes a modifier, post-marketing surveillance demonstrates prescribers and other healthcare provider may omit the modifier when writing a prescription or medication order. Adding to our concern is the fact the injection form of Aloxi would not utilize a modifier, thus suggesting to healthcare providers, that the use of the modifier is unnecessary. We believe the omission of the modifier would likely lead to the name confusion errors as described in Section 4.1 of this discussion. Therefore, we believe the addition of a modifier would minimally reduce the potential for name confusion medication errors.

Our Division believes the use of modifiers in this circumstance has the potential to contribute to medication errors. Modifiers have lead to confusion of meaning of the modifier, confusion with other modifiers, and confusion with the route of administration leading to medication errors. Depending on what the Applicant would choose as a modifier any of these potential sources of errors could result. Therefore, our Division believes modifiers, in general, are likely to contribute to medication errors unless no other possible means of minimizing risk is an option.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Aloxi, does appear to be vulnerable to name confusion that could lead to medication errors. Although this finding would typically lead the Division of Medication Error Prevention and Analysis to object to the proposed proprietary name, FMEA of alternatives approaches to address this name confusion, including a new name for palonosetron capsules, a new name for all palonosetron HCL products, or use of a modifier with the name, also found potential opportunities for medication errors. Moreover, FMEA of Aloxi found that two of the products which will likely be confused with Aloxi are for external use only, thus they have a better detectability prior to reaching the patient compared to the alternative approaches. In addition, the Agency has received no reports of medication errors resulting from name confusion with currently marketed Aloxi. Therefore, the medication error prevention staff does not object to the use of the proprietary name, Aloxi, for this product as modifications or alternative names to an existing proprietary name were also found to result in medication errors.

However; if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and the name must be

resubmitted for re-review. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Applicant to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

5.1 COMMENTS TO THE DIVISION

The Division of Medication Error Prevention and Analysis would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Cheryle Milburn, project manager, at 301-796-2084.

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name Risk Assessment

The Proprietary Name Risk Assessment findings indicate that the proposed name, Aloxi, does appear to be vulnerable to name confusion that could lead to medication errors. Specifically, we identified potential name confusion with the existing products, Adoxa, Alora and Olux-E. Although this finding would typically lead the Division of Medication Error Prevention and Analysis to object to the proposed proprietary name, a Failure Mode and Effects Analysis of alternatives approaches to address this name confusion, including a new name for palonosetron HCl capsules, a new name for all palonosetron HCL products, or use of a modifier with the name, also found potential opportunities for medication errors. Moreover, FMEA of Aloxi found that two of the products which will likely be confused with Aloxi are for external use only, thus have a better detectability prior to reaching the patient compared to the alternative approaches. Therefore, the medication error prevention staff does not objects to the use of the proprietary name, Aloxi, for this product as modifications or alternative names to an existing proprietary name were also found to result in medication errors.

6 REFERENCES

6.1 REVIEWS

- 1. OSE Review # 02-0068, Proprietary Name Review of Aloxi and Cinvex; Hoppes, C.; July 16, 2002.***
- 2. OSE Review # 02-0068-2, Proprietary Name Review of Cinvex; Hoppes, C.; March 18, 2003.***
- 3. OSE Review #2006-1128. Proprietary Name, Label and Labeling Review of Olux-E, Pedersen, K.; January 10, 2007.***

6.2 DATABASES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential post-marketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

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

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

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

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. This is a database which was created for the medication error prevention staff, FDA.

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

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

5. *AMF Decision Support System [DSS]*

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

6. *Division of Medication Error Prevention and Analysis proprietary name consultation requests*

This is a list of proposed and pending names that is generated by the medication error prevention staff from the Access database/tracking system.

7. *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](#) and [generic drugs](#) and [therapeutic biological products](#); [prescription](#) and [over-the-counter](#) human drugs and [therapeutic biologics](#), [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

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

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. US Patent and Trademark Office location (<http://www.uspto.gov>)

Provides information regarding patent and trademarks.

10. Clinical Pharmacology Online (<http://www.clinicalpharmacology-ip.com/>)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. 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 tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. Natural Medicines Comprehensive Databases (<http://www.naturaldatabase.com>)

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

13. Stat!Ref (<http://www.statref.com/>)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

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

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

16. Lexi-Comp (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The medication error prevention staff also compares the spelling of the proposed proprietary name with the proprietary and established 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. The Medication Error Staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the medication error prevention staff will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, the medication error prevention staff also considers a variety of pronunciations that could occur in the English language.

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 Downstrokes	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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

Appendix B:

CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Aloxi	Aloxi	Alaw
Aloxi	Aloxi	Aloxi
Aloxi	Aloxy	Alva
Aloxi	Aloxi	Alotri
Aloxi	Aloxi	Alori
Aloxi	Aloxy	Aloi
Aloxi		Alva
Aloxi		Alavi
Aloxi		Aloxi
Aloxi		Alavi

Aloxi		

Appendix C: Proprietary names with minimal orthographic or phonetic similarity

Proprietary Name	Similarity to Aloxi
Avelox®	Look
Droxy®	Sound
Lanoxin®	Look and Sound
M-oxy®	Look and Sound
Roxicet®	Look and Sound

Appendix D: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Aloxi	Country
Alax	Look	Poland
Alaxa	Look and Sound	Italy
Aloxyn	Sound	Germany

Appendix E: Proprietary names of non-medication products used in healthcare settings

Proprietary Name	Similarity to Aloxi	What the product was identified as
Celox®	Look	Device- powder used by emergency responders to stop bleeding in trauma victims (including military use).
Cidex®	Look	Product line of disinfectant solutions used for the sterilization of materials.

Appendix F: Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Aloxi® (Palonosetron HCl) Capsules		0.5 mg capsules (already marketed as 0.25 mg and 0.075 mg injection)	Usual dose: 0.5 mg one hour prior to the start of chemotherapy
Abreva®	Look	10 %	Apply five times daily.
Alocril®	Look	2 %	One to two drops in each eye twice a day.
Alomide®	Look and Sound	0.1 %	One to two drops in affected eye four times daily.
Cedax®	Look	90 mg/5 mL and 400 mg	400 mg daily or 9 mg/kg daily for pediatric patients.
Celexa®	Look	10 mg, 20 mg and 40 mg	One tablet daily.
Celontin®	Look	150 mg and 300 mg	Two capsules twice daily.
Ciloxan®	Look	0.3 %	Two drops every two hours or apply ointment twice to three times daily.
Floxin®	Look	200 mg, 300 mg and 400 mg and 0.3% Otic	One tablet every 12 hours.

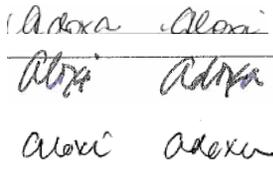
Appendix G: Potential confusing names with overlapping strength or dose

Aloxi® (Palonosetron Hydrochloride)	0.5 mg capsule	Usual dose: 0.5 mg one hour prior to the start of chemotherapy
Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>Aleve® (naproxen sodium) 200 mg tablets, liquid gels, smooth gels and caplets</p>	<p>Orthographic similarity: each begins with ‘Al’, each contains five letters, and the ending ‘e’ appears similar to ‘i’ when scripted.</p> <p>Both are available as an oral solid dosage form (tablet vs. capsule) in one strength. Therefore, the strength may be omitted from a prescription.</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The center letters, ‘ev’ in Aleve, provide orthographic differences compared to ‘ox’ in Aloxi as they lack a cross-stroke included in the ‘x.’</p> <p>Aleve is a nonprescription form of naproxen sodium available in several oral dosage forms (tablets, liquid gels, smooth gels and caplets).</p> <p>Naproxen sodium is available in several strengths under different proprietary names.</p> <p>The quantities available, the indications for use, and the prescribers differ, as well.</p>
<p>Alesse® (ethinyl estradiol/ levonorgesterel) 20 mcg/0.1 mg tablets</p>	<p>Orthographic similarity: Both begin with ‘Al’ and the ending letter ‘e’ is similar to ‘i’ when written.</p> <p>Phonetic similarity: Both begin with same sound, ‘Al-.’</p> <p>Both are available as an oral solid dosage form (tablet vs. capsule) in one strength. Therefore, the strength may be omitted from a prescription.</p> <p>Both may be prescribed “Use as directed.”</p>	<p>Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>Orthographic differences stem from the middle letters of each name. The ‘ess’ in Alesse provides an additional letter and length and lacks a cross stroke when compared to Aloxi. The phonetic differences are provided by the fact that Alesse has only two syllables compared to Aloxi which has three. The added and last syllable in Aloxi being the vowel sound ‘ee.’</p> <p>The available quantities, the indications for use, and the prescribers differ, as well.</p>

<p>Alli® (orlistat) 60 mg capsules</p>	<p>Orthographic similarity: Both begin with 'Al'; both end with the letter 'i.'</p> <p>Phonetic similarity: Both begin with same sound, 'Al-'</p> <p>Both capsules are available in one strength. Therefore, the strength may be omitted from a prescription.</p> <p>Dose can be one capsule.</p>	<p>Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The 'ox' in Aloxi provides orthographic and phonetic differences compare to Alli. Orthographic differences include an additional letter and length in the name, no second upstroke, and a cross stroke provided by the 'x.' Phonetic differences include additional syllable (3 vs. 2) and the '-cks' provided by the 'x.'</p> <p>Alli is a nonprescription product which does not require a written prescription.</p> <p>The available quantities, the indications for use, and the prescribers differ, as well.</p>
<p>Aloprim® (allopurinol sodium) for injection 500 mg</p>	<p>Orthographic similarity: Both begin with 'Alo' and both include an 'i' near the end of the name.</p> <p>Phonetic similarity: Both begin with 'Alo-' and both have three syllables.</p> <p>Share numerically similar strengths (500 mg vs. 0.5 mg)</p> <p>Share prescribers (oncologists)</p>	<p>Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The orthographic differences stem from the additional letters in the name Aloprim. Two letters between the 'o' and the 'i' as well as the 'm' on the end of the name provide added length. Phonetic differences are provided by the additional letters as well, the third syllable of Aloprim starts with a 'pr-' sound compared to the 'cks' sound in Aloxi and end with a 'mm' sound while the third syllable in Aloxi has no ending consonant sound.</p> <p>While the strengths are similar, the dose of Aloprim is based on mg/m² and minimizes the risk of the dose to overlap.</p>
<p>Amoxil® (Amoxicillin) 250 mg and 500 mg capsules 875 mg tablets 200 mg and 400 mg chewable tablets 50 mg/mL, 200 mg/5 mL, 250 mg/5 mL, and 400 mg/5 mL powder</p>	<p>Orthographic similarity: Both begin with 'A'; Both have 'oxi' in the third, fourth and fifth positions, respectively; and both contain the letter 'l.'</p> <p>Phonetic similarity: both contain three syllables; First syllable is 'Ah-'; and second syllable contains the sound 'ox.'</p> <p>Share a numerical similar</p>	<p>Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>Orthographic differences stem from the fact the second letter in Amoxil is an 'm' compared to an 'l' in Aloxi as well as the fact the 'l' in Amoxil is the last letter in the name. The ending letter 'l' provides some phonetic differentiation by providing a consonant sound at the end of the name.</p> <p>Amoxil is available many strengths and dosage forms</p>

for oral suspension	<p>strength (500 mg and 50 mg/mL vs. 0.5 mg)</p> <p>Dose can be one oral solid dosage form (tablet or capsule vs. capsule).</p>	<p>which must be specified for prescriptions or medication orders to be filled.</p> <p>Frequency of administration for Amoxil must be specified as it may be taken twice or three times daily and neither of these frequencies overlaps with Aloxi.</p>
<p>Eloxatin® (oxaliplatin) 50 mg/10 mL, 100 mg/20 mL and 200 mg/40 mL vials</p>	<p>Phonetic similarity: First syllable is a vowel sound, second syllable is the same '-lox-' and the third is a vowel sound.</p> <p>Share numerically similar strengths (50 mg vs. 0.5 mg)</p> <p>Share patient populations (cancer patients)</p> <p>Share prescribers (oncologists)</p>	<p>Phonetic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The phonetic difference stems the fourth syllable '-tin' in Eloxatin.</p> <p>The dose of Eloxatin is 85 mg/m², and therefore the overlap in dose is unlikely.</p> <p>As Eloxatin is a chemotherapy agent, few institutions or clinics allow for verbal orders for this type of medication.</p>

Appendix H: Failure Mode and Effects Analysis for problematic names

Aloxi® (Palonosetron Hydrochloride)	0.5 mg capsule	Usual dose: 0.5 mg one hour prior to the start of chemotherapy		
Failure Mode: Name confusion	Causes	Effects	Detectability	Regulatory approaches to managing this risk
<p>Adoxa® (doxycycline) 50 mg, 75 mg, 100 mg, and 150 mg tablets</p>  <p>The image shows three handwritten comparisons of the names 'Adoxa' and 'Aloxi'. The first shows 'Adoxa' and 'Aloxi' side-by-side. The second shows 'Aloxi' and 'Adoxa' side-by-side. The third shows 'Aloxi' and 'Adoxa' side-by-side, with the 'ox' in 'Aloxi' and 'Adoxa' underlined to highlight the similarity.</p>	<p>Orthographic similarity: Both begin with 'A'; both contain five letters, the second letter provides an upstroke (d vs. l); and the third and fourth letters are the same 'ox'.</p> <p>Phonetic similarity: Both begin with 'Ah-'; both contain three syllables; and the second syllable contains '-ox.'</p> <p>The products share numerically similar strengths (50 mg vs. 0.50 mg).</p> <p>The products are both oral solid dosage forms (tablet vs.</p>	<p>Wrong product medication error resulting from confusion between the names.</p> <p>The wrong product could be ordered from wholesaler or selected from drop-down screen at order entry when prescription is filled.</p> <p>The patient would not receive antiemetic therapy needed for moderately emetogenic therapy. Instead, the patient would receive a medication that causes nausea and vomiting (doxycycline).</p> <p>A patient receiving Aloxi instead of Adoxa would have infection go untreated.</p>	<p>Low: Patient would receive a product which is an oral solid even if error is made.</p> <p>The usual directions for use differ: Adoxa 50 mg- One tablet (50 mg) po every six hour on the first day then one tablet (50 mg) po every twelve hours.</p> <p>If the patient receives patient counseling from the pharmacist at the time of dispensing, the patient may be able to identify product is incorrect based on the indication.</p> <p>The quantity requested to dispense for Adoxa may be higher as Adoxa therapy lasts one to two weeks.</p> <p>Potential nausea and vomiting caused by an error</p>	<p>Use an alternative name for the oral formulation of palonosetron HCl.</p> <p>Use an alternative proprietary name for all palonosetron products from the Applicant.</p> <p>Add a modifier to the name to identify the oral formulation.</p>

	<p>capsule.)</p> <p>Both may have directions for use written as ‘Take one po daily’ or ‘Use as directed’</p> <p>Both will be dispensed from outpatient pharmacies.</p> <p>The quantity may overlap if several courses of Aloxi capsules are written for as one prescription.</p>		<p>of Adoxa received instead of Aloxi may be attributed to anticipatory nausea and vomiting related to the chemotherapy.</p>	
<p>Alora® (estradiol) 0.025 mg, 0.05 mg, 0.075 mg, and 0.1 mg Transdermal systems</p> <p><i>Alora Aloxi</i></p> <p><i>Alora Aloxi</i></p> <p><i>Alora Aloxi</i></p>	<p>Orthographic similarities: Both begin with same three letters, ‘Alo’ both contain a total of five letters; when scripted, the letters ‘ri’ may appear similar to ‘xa.’</p> <p>The products share numerically similar strengths (0.05 mg vs. 0.50 mg).</p> <p>Both may have</p>	<p>Wrong product medication error resulting from confusion between the names.</p> <p>The wrong product could be ordered from wholesaler or selected from drop-down screen at order entry when prescription is filled.</p>	<p>Moderate: Patient or caregiver may be able to identify that an incorrect dosage form was dispensed prior to using it.</p> <p>Patient counseling at time of dispensing may help identify the medication error.</p>	<p>Use an alternative name for the oral formulation of palonosetron HCl.</p> <p>Use an alternative proprietary name for all palonosetron products from the Applicant.</p> <p>Add a modifier to the name to identify the oral formulation.</p>

	<p>directions for use written as ‘Use as directed.’</p> <p>Both will be dispensed from outpatient pharmacies.</p> <p>These products are packaged in differing quantities, five capsules for Aloxi and eight patches for Alora. However when written, five and eight can appear similar.</p> <p>A prescription for a small quantity of Aloxi (one or two) may be interpreted as the number of month’s supply.</p>			
<p>Olux-ETM (clobetasol propionate) 0.05% foam</p>	<p>Phonetic similarity: Both names have begin with similar sounding vowels (‘Oh-’ vs. ‘Ah-’); both contain three syllables, the second and third syllables</p>	<p>These names sound nearly identical when spoken. A verbal prescription would result in a wrong product medication error.</p> <p>If, the verbal prescriptions left on voice mail system the pharmacists will be unable to read back or</p>	<p>Moderate: Patient or caregiver may be able to identify that an incorrect dosage form was dispensed prior to using it.</p> <p>Patient counseling at time of dispensing would help</p>	<p>Use an alternative name for the oral formulation of palonosetron HCl.</p> <p>Use an alternative proprietary name for all palonosetron</p>

	<p>sound nearly identical when spoke ('lucks-ee' vs. 'locks-ee').</p> <p>Share numerically similar strengths (0.05% vs. 0.50 mg).</p> <p>Olux-E is available in one container size (100 gram) allowing for similarly small dispensing quantities (one or two).</p> <p>Both may have directions for use given as 'Use as directed.'</p> <p>Both will be dispensed from outpatient pharmacies.</p>	<p>clarify the prescription.</p> <p>Wrong product is transcribed from the verbal order to writing by pharmacist.</p>	<p>identify the medication error.</p>	<p>products from the Applicant.</p> <p>Add a modifier to the name to identify the oral formulation.</p>
Use of an Alternative Proprietary name				
Failure Mode: Unidentified oral antiemetic therapy	Causes	Effects	Detectability	Managing the Risk
New proprietary name for oral formulation	Unrecognized proprietary name of oral palonosetron HCl when medication reconciliation is	Prescribers unaware an oral dose of palonosetron was administered prior to arriving for chemotherapy treatment would order an intravenous dose of Aloxi. Patient	Low: This error is unlikely to be detected before it occurs.	Allow Aloxi as the name for the oral formulation. Recommend change

	completed. Healthcare providers unaware that palonosetron is available as an oral formulation as well as an injectable formulation.	would receive a dose of palonosetron injection prior to treatment resulting in a duplicate therapy medication error. Duplicate therapy leads to overdoses of palonosetron and likely increase the risk of adverse events related to palonosetron.		the proprietary name of all palonosetron products produced by the applicant.
New proprietary name for all palonosetron products.	Healthcare providers familiar with the proprietary name, Aloxi, unaware the proprietary name has been changed and continues to write for Aloxi for the injectable form of palonosetron HCl.	Prescribers unaware an oral dose of palonosetron was administered prior to arriving for chemotherapy treatment would order an intravenous dose of Aloxi. Patient would receive a dose of palonosetron injection prior to treatment resulting in a duplicate therapy medication error. Duplicate therapy leads to overdoses of palonosetron and likely increase the risk of adverse events related to palonosetron.	Low: Inpatient pharmacist and other healthcare providers are more likely to recognize the name, Aloxi. At launch of oral capsules, many inpatient pharmacies and drug wholesalers will have a sizable quantity of Aloxi injection vials available.	Allow Aloxi for all palonosetron products. Use a modifier for the oral product.
Use of a modifier with the name Aloxi for the oral capsule formulation				
Failure Mode: Lack of modifier use	Causes	Effects	Detectability	Managing the Risk
Healthcare providers fail to use modifier.	A modifier is not required for all dosage forms of Aloxi.	Name confusion medication errors are likely to occur with the three names(Adoxa, Alora, and Olux-E as noted above.	See Adoxa, Alora, and Olux-E above.	Use an alternative name for the oral formulation of palonosetron HCl.

	Prescribers may forget to use the modifier.			<p>Use an alternative proprietary name for all palonosetron products from the Applicant.</p> <p>Recommend education healthcare providers regarding the need to use a modifier with the name Aloxi for the oral formulation.</p> <p>Allow Aloxi for all palonosetron products without a modifier.</p>
Modifiers are confused with other portions of the prescription	Modifier is misinterpreted by healthcare providers as an inappropriate strength, route of administration or frequency of administration.	Result in medication errors of wrong dose, wrong route of administration, wrong frequency of use or extra dose.	Low: Patient counseling from the pharmacist at the time of dispensing may identify the error.	<p>Recommend education healthcare providers regarding the need to use a modifier with the name Aloxi for the oral formulation and what the modifier means.</p> <p>Allow Aloxi for all palonosetron products without a modifier.</p>

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/s/

Kellie Taylor
8/6/2008 04:34:42 PM
DRUG SAFETY OFFICE REVIEWER
signing on behalf of Rick Abate, Denise Toyer, and
Carol Holquist