CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-244

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:	December 11, 2008
To:	Bob Rappaport, MD, Director Division of Analgesics, Anesthetics and Rheumatology Products
Through:	Kristina Arnwine, PharmD, Acting Team Leader Denise Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis
From:	Anne Crandall, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name:	Lusedra (Fospropofol Disodium) Injection 1,050 mg/30 mL (25 mg/mL)
Application Numbers:	NDA 22-244
Applicant:	MGI Pharma
OSE RCM #s:	2008-1909

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Analgesia, Anesthesia and Rheumatology Products for a re-assessment of the proposed proprietary Lusedra. This review will be an abbreviated version of the standard pre-action proprietary name review due to the time constraints brought about by the impending PDUFA date of December 12, 2008

1.2 REGULATORY HISTORY

In our previous review (2008-579, dated July 7, 2008) we had no objection to the proposed proprietary name, Lusedra. A separate label and labeling review (2008-1743, dated November 26, 2008) was completed by the Division of Medication Error Prevention and Analysis, and will not be discussed in this review.

2 METHODS

We applied the same search criteria that we utilize in our usual proprietary name review to identify any proprietary names that look or sound alike to the proposed name, Lusedra. The website Drugs@FDA was searched for proprietary names that have been approved since the July date of the initial proprietary name review for the potential for name confusion resulting in medication errors.

3 RESULTS

One proprietary name, Inspra, was identified in this search as a name that could result in medication errors due to name confusion. Failure modes and effects analysis (FMEA) was applied to determine if the proposed name, Lusedra, could be confused with Inspra (see Appendix A).

The results of the FMEA found that proposed name, Lusedra, is not vulnerable to name confusion that would lead to medication errors.

4 CONCLUSIONS AND RECOMMENDATIONS

We have completed our abbreviated re-assessment of the proposed proprietary name, Lusedra, and do not object to the use of the name.

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Chris Wheeler, Project Manager, at 301-796-0151.

Appendix A: 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)
Lusedra (Fospropofol disodium) Injection		**1,050 mg/30 mL (35 mg/mL) single use vial**	**Initial intravenous bolus of 6.5 mg/kg followed by supplemental dosages of 1.6 mg/kg as needed (for patients weighing less then 60 kg, patient should be dosed as if they are 60 kg, for patients weighing more then 90 kg, dose as if 90 kg)**
Inspra (Eplerenone) tablet	Look-Alike	25 mg, 50 mg oral tablet	Congestive Heart Failure Post-Myocardial Infarction: initiate treatment with 25 mg orally once daily, may increase up to 50 mg orally once daily after 4 weeks Hypertension: 50 mg orally once daily, for inadequate response may increase up to 50 mg orally twice a day

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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:	July 7, 2008
To:	Bob Rappaport, M.D., Director Division of Anesthesia, Analgesia, and Rheumatology Products, HFD-170
Through:	Linda Kim-Jung, Pharm.D., Team Leader Denise Toyer, Pharm.D., Deputy Director Division of Medication Error Prevention, HFD-420
From:	Tara Turner, Pharm.D., Safety Evaluator Division of Medication Error Prevention, HFD-420
Subject:	Proprietary Name Review
Drug Name(s):	Lusedra (Fospropofol Disodium) Injection 1,050 mg/30 mL (35 mg/mL)
Application Type/Number:	NDA # 22-244
Applicant:	MGI Pharma
OSE RCM #:	2008-579

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CONTENTS

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Lusedra, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention does not object to the use of the proprietary name, Lusedra, for this product at this time.

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 recommend that the name and its associated labels and labeling be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Anesthesia, Analgesia, and Rheumatology Products (HFD-170) for assessment of the proprietary name, Lusedra, regarding potential name confusion with other proprietary or established drug names. Revised container labels, carton and insert labeling were not submitted for review and comment.

1.2 REGULATORY HISTORY

The Division of Medication Error Prevention objected to the applicant's primary name, Aquavan (see OSE Review #2007-2189, dated May 8, 2008) b(4)

Additionally, the container labels, carton and insert labeling were evaluated as part of that review. Lusedra is the applicant's alternate name choice (secondary).

1.3 PRODUCT INFORMATION

Lusedra (fospropofol disoodium) is an intravenous sedative-hypnotic agent indicated for sedation in adult patients undergoing diagnostic or therapeutic procedures. b(4)

The dosage of Lusedra should be individualized and titrated to the level of sedation required for the procedure. Lusedra is administered intravenously as a bolus injection. The standard dosing regimen is an initial dose of 6.5 mg/kg with supplemental doses of 1.6 mg/kg (25% of the initial dose) as needed to achieve the desired level of sedation. The dosage of Lusedra is limited by lower and upper weight bounds of 60 kg and 90 kg, respectively. Adults who weigh more than 90 kg should be dosed as if they are 90 kg; adults who weigh less than 60 kg should be dosed as if they are 60 kg. No initial dose should exceed 16.5 mL and no supplemental dose should exceed 4 mL.

Lusedra will be available in a 35 mg/mL concentration and supplied in single-use glass vials containing 30 mL, ready for intravenous injection. Lusedra should be stored at room temperature 20°C to 25°C (68°F to 77 °F).

2 METHODS AND MATERIALS

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Lusedra, 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, Lusedra, the medication error staff searches a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Section 2.1 for detail) and holds an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.2). We also conduct internal CDER prescription analysis studies (see Section 2.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.3). 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. We use the clinical expertise of the medication error staff 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, we consider the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2]

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

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

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

For this review, particular consideration was given to drug names beginning with the letter 'L' 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.[3,4]

To identify drug names that may look similar to Lusedra, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two, capital letter 'L' and lower case 'd'), downstokes (none), cross-strokes (none) and dotted letters (none). Additionally, several letters in Lusedra may be vulnerable to ambiguity when scripted, including the capital letter 'L' may appear as capital 'Z', 'C', 'F' or 'T'; lower case 'u' may look like lower case 'a', 'e', 'o', 'v', 'y', 'n' or 're'; lower case 's' may look like lower case 'n', 'a', or 'o'; lower case 'e' may look like lower case 'a', 'u', 'i', 'o', or 'l'; and lower case 'd' may appear as lower case 'cl'; lower case 'r' may appear as lower case 'n' or 'i'; and lower case 'a' may appear as lower case 'c', 'ce', 'ci', or 'o'. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Lusedra.

When searching to identify potential names that may sound similar to Lusedra, the Medication Error Staff search for names with similar number of syllables (3), stresses (lu-SE-dra, LU-se-dra or lu-se-DRA), and placement of vowel and consonant sounds. In addition, several letters in Lusedra may be subject to interpretation when spoken, including the letters 'se' may be interpreted as 'si'; the letter 's' may be interpreted as 'c'; and the letter 'd' may be interpreted as 't'. The Applicant's intended pronunciation of the proprietary name is "loo-seed-rah".

The Staff also consider 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 Staff were provided with the following information about the proposed product: the proposed proprietary name (Lusedra), the established name (fospropofol disodium), proposed indication (sedation in adult patients undergoing diagnostic or therapeutic procedures; [redacted] strength (1,050 mg/30 ml vial), dose (initial dose of 6.5 mg/kg with supplemental doses of 1.6 mg/kg), frequency of administration (as needed to achieve the desired level of sedation), route (intravenous), and dosage form (solution). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration. b(4)

Lastly, the Medication Error Staff also consider 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 Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and information sources

The proposed proprietary name, Lusedra, was provided to the medication error 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 Lusedra using the criteria outlined in 2.1. A standard description of the databases used in the searches is provided in Section 7. To

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

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

complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review 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.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Lusedra. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of 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.

2.1.2 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 Lusedra 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 Lusedra in handwriting and verbal communication of the name, inpatient medication orders are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and delivered to a random sample of 123 participating health professionals via e-mail. In addition, a verbal medication order 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 medication orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

Figure 1. Lusedra Study (conducted on April 29, 2008)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order #1: Lusedra give IV bolus of 442mg prior to surgery	"Lusedra Give an IV bolus dose of 442 mg prior to surgery"
Inpatient Medication Order #2: Lusedra 442mg IV bolus prior to surgery	

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2, 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.[5]

When applying FMEA to assess the risk of a proposed proprietary name, we seek 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 then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the 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 Lusedra 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 Lusedra 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

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

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.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when 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. We identify 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. Medication Error Staff identify 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 we object 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 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 we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission, and the Institute for Safe Medication Practices, who 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, we contend 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 Sponsor, 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 Sponsor'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, we believe 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 we object 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. We are likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for us 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 Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

We conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Lusedra to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, twenty-two names were identified as having some similarity to the name Lusedra: Luveria, Lusedan, Levitra, Apidra, Lutera, Lusonex, Ceredrase, Posurdex, Lysodren, Lustre, Lasix, Leziva, Leptandra, Sustiva, Lucipral, Ephedra, Lunesta, Loestrin, Lustra, Losartan, Lucentis, and Lukestra.

Fourteen of the twenty-two names were thought to look like Lusedra (Luveris, Lusedan, Levitra, Apidra, Lutera, Lusonex, Ceredrase, Posurdex, Lysodren, Lustre, Lasix, Laziva, Leptandra, and Sustiva). One name (Lucipral) was thought to sound like Lusedra. The remaining seven names (Lunesta, Loestrin, Lustra, Losartan, Lucentis, Lukestra, and Ephedra) were thought to look and sound similar to Lusedra.

Additionally, the Division of Medication Error Prevention did not identify any USAN stems in the name, Lusedra, as of April 10, 2008.

3.1.2 Expert panel discussion

The Expert Panel reviewed the pool of names identified by Medication Error Prevention staff (see section 3.1 above) but did not identify any additional names with similarity to Lusedra. During the discussion the Expert Panel posed the following questions regarding the drug product:

Is this dosing similar to propofol?

Is the sponsor the same?

Is this formulation white like propofol?

In response, we note the following: the dosing for Lusedra is weight based, but it requires a different mg/kg amount than propofol; the Lusedra sponsor (MGI Pharma) is different from the sponsors of the brand and generic propofol products; Lusedra is a clear, colorless solution.

Additionally, the Expert Panel recommended that the primary safety evaluator ensure that the labeling is differentiated from that of propofol. In response, we note that the labeling review for this product was included in OSE Review #2007-2189. The labeling for Lusedra does not resemble that of Diprivan or generic propofol labels and labeling.

DDMAC had no concerns regarding the proposed name from a promotional perspective. DDMAC posed a safety concern that Lusedra looks and sounds similar to Lunesta.

However, the Expert Panel expressed concern that the name Lusedra sounds like "lucid" and that the name may imply that a person will be lucid upon awakening from anesthesia. We requested that DDMAC re-evaluate the name. DDMAC responded via e-mail dated April 11, 2008 and indicated that they discussed the possible connection between "Lusedra and "lucid" but they "feel that it is too much of a stretch to form an objection to the proposed trade name."

3.1.3 CDER Prescription Studies

A total of 28 practitioners responded. About 78% of the participants (n=22) interpreted the name correctly as "Lusedra", with the correct interpretation occurring more frequently in the written inpatient study #2. The remainder of respondents misinterpreted the drug name. The most common misinterpretation involved transcription of the letter 'c' instead of the letter 's'. All 4 participants in the verbal study, as well as one participant in the written inpatient study #1, made this error. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety evaluator risk assessment

The primary Safety Evaluator, affording careful evaluation to drug names beginning with the letters 'L' 'Z', 'F', 'S', 'C', and 'T', conducted independent searches which identified seven additional names with similarity to Lusedra. The names identified to have look-alike similarities are: Lusert, Lusonal, Sustaire, and Luden's throat drops. The names identified to have look-alike and sound-alike similarities are: [redacted] b(4)
Additionally, we note that attempts to identify the drug names Ceredrase and Leziva were unsuccessful. We assume that these names were misspelled during the search process. Thus, we evaluated Ceredase and Lexiva, respectively. As such, a total of twenty-nine names were analyzed to determine if the drug names could be confused with Lusedra and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Lusedra, and thus determined to present some risk for confusion. Failure modes and effects analysis (FMEA) was then applied to determine if the proposed name, Lusedra, could potentially be confused with any of the twenty-nine names and lead to medication error.

This analysis determined that the name similarity between Lusedra and the identified names was unlikely to result in medication errors for any of the twenty-nine products. Four names were not considered further because they lack convincing orthographic and/or phonetic similarities with Lusedra. The names are Posurdex, Lasix, Leptandra, and Lucipral (see Appendix C). Two names (Lusedan and Lusert) are drug products marketed in foreign countries (see Appendix D). Three names ([redacted] b(4)
) are proposed proprietary names for other products within the Agency which were not approved or were approved under a different proprietary name (see Appendix E). One name, [redacted] is a pending name which is currently under review within the Agency. However, medication errors resulting from confusion with this product are unlikely because Lusedra has individualized dosing based on the patient's weight as opposed to the usual dose of one tablet for [redacted] Two names (Lustre and Luden's throat drops) are for over-the-counter products with a different context of use than Lusedra (see Appendix F). One name, Ephedra, is a natural medicine product with a different context of use than Lusedra. According to the Natural Medicines Comprehensive Database, Ephedra is banned in the U.S.

Ten names (Levitra, Lusonex, Sustiva, Loestrin, Losartan, Lusonal, Apidra, Ceredase, Lexiva, and Sustaire) are products with no overlap in strength or dosage with Lusedra (see Appendix G). We note that Sustaire has been discontinued as a brand name generic product and is no longer available in the U.S. Although other generic theophylline extended release products are available, the route of administration and frequency differences will help differentiate these two products. The remaining six names (Luveris, Lutera, Lysodren, Lunesta, Lustra, and Lucentis) have strong orthographic similarities to Lusedra, despite a lack of overlap in strength or dosage. However, analysis of the failure modes did not determine the effects of these similarities to result in medication errors in the usual practice setting (see Appendix H).

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

The results of the Proprietary Name Risk Assessment found that the proposed name, Lusedra, has some similarity to twenty-nine other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Lusedra, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention does not object to the use of the proprietary name, Lusedra, for this product at this time.

5.1 COMMENTS TO THE DIVISION

The Division of Medication Error Prevention does not object to the use of the proprietary name, Lusedra, for this product at this time. 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 recommend that the name be resubmitted for review. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy us on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Darrell Jenkins, project manager, at 301-796-0558.

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name

1. The Division of Medication Error Prevention does not object to the use of the proprietary name, Lusedra, for this product at this time.
2. 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 recommend that the name be resubmitted for review.

6 REFERENCES

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 postmarketing 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://weblern/)

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 Division of Medication Error Prevention, FDA.

4. Drug Facts and Comparisons, online version, St. Louis, MO (http://weblern/)

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 proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention 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 biologicals, 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. United States Patent and Trademark Office http://www.uspto.gov.

Provides information regarding patent and trademarks.

10. Clinical Pharmacology Online (http://weblern/)

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://weblern/)

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

13. Stat!Ref (http://weblern/)

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. We also compare 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 (e.g.,"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, we will consider the Sponsor's intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, we also consider 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	• 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 Cross-strokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B:

Lusedra Prescription Study Responses

Inpatient Medication Order #1	Inpatient Medication Order #2	Voice Prescription
Lucedra	Lusedra	Lucedra
Lusedra	Lusedra	Lucedra
Lusedra	Lusedra	Lucedra
Lusedra	Lusedra	Lucedra
Lusedra	Lusedra	
Lusedra	Lusedra	
Lusedra	Lusedra	
Lusetra	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	
	Lusedra	

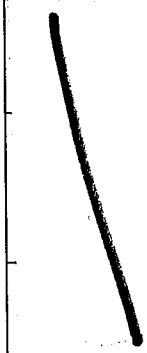
Appendix C: Names lacking convincing look-alike or sound-alike similarities with Lusedra

Proprietary Name	Similarity to Lusedra
Posurdex	Look
Lasix	Look
Leptandra	Look
Lucipral	Sound

Appendix D: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Lusedra	Country	Description
Lusedan	Look	Venezuela	sertraline
Lusert	Look	Ireland	sertraline

Appendix E: Proposed proprietary names for products not approved or approved with another name

Proprietary Name	Similarity to Lusedra	Status
	Look and Sound	Withdrawn by Commissioner 8/6/1971
	Look and Sound	Name found acceptable; application withdrawn unapproved (WU)
	Look and Sound	Name found unacceptable; product approved as

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Appendix F: Over-the-Counter Products

Proprietary Name	Similarity to Lusedra	Description
Lustre	Look	Natural medicine product
Luden's throat drops	Look	Family name of lozenges for sore throat/sore mouth; contains either pectin or menthol

Appendix G: Products with no numerical overlap in strength or dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Lusedra (fospropofol disodium) injection		**1,050 mg/30 mL vial (35 mg/mL)**	**Initial intravenous bolus dose of 6.5 mg/kg followed by supplemental dosages of 1.6 mg/kg as needed**
Levitra (vardenafil hydrochloride) tablets	Look	2.5 mg, 5 mg, 10 mg, 20 mg	10 mg orally approximately 60 minutes before sexual activity
Lusonex (guaifenesin/phenylephrine) tablets	Look	800 mg guaifenesin/ 20 mg phenylephrine	One tablet orally every 12 hours
Sustiva (efavirenz) tablets and capsules	Look	Tablets: 600 mg Capsules: 50 mg, 100 mg, 200 mg	600 mg orally once daily
Loestrin (norethindrone/ethinyl estradiol) tablets	Look and Sound	Loestrin 21 1/20 (1 mg/0.02 mg) Loestrin 21 1.5/30 (1.5 mg/0.03 mg) Loestrin 24 FE (24 tabs of 1 mg/0.02 mg + 4 tablets of 75 mg ferrous fumarate) Loestrin FE 1/20 (21 tabs of 1 mg/0.02 mg + 7 tabs of 75 mg ferrous fumarate) Loestrin FE 1.5/30 (21 tabs of 1.5 mg/0.03 mg + 7 tabs of 75 mg ferrous fumarate)	One tablet orally once daily

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Lusedra **(fospropofol disodium) injection**		**1,050 mg/30 mL vial** **(35 mg/mL)**	**Initial intravenous bolus dose of 6.5 mg/kg followed by supplemental dosages of 1.6 mg/kg as needed**
Losartan Trade names: Cozaar and Hyzaar	Look and Sound	Cozaar (losartan): 25 mg, 50 mg, 100 mg Hyzaar (losartan/hydrochlorothiazide): 50 mg/12.5 mg 100 mg/12.5 mg 100 mg/25 mg	Cozaar: 50 mg orally once daily Hyzaar: 50 mg/12.5 mg orally once daily
Lusonal (phenylephrine) oral liquid	Look	7.5 mg/5 mL	10 mL orally every 6 hours; up to 40 mL per day
Apidra (insulin glulisine recombinant) injection	Look	100 units/mL: 10 mL vial or 3 mL cartridge system	Individualized dosing
Ceredase (alglucerase) injection	Look	80 units/mL: 400 units/5 mL bottle	Initial dosage may be as little as 2.5 units/kg 3 times a week up to as much as 60 units/kg administered as frequently as once a week or as infrequently as every 4 weeks; 60 units/kg every 2 weeks is the dose for which the most data are available
Lexiva (fosamprenavir calcium)	Look	Tablets: 700 mg Oral Suspension: 50 mg/mL	Therapy-naïve adults: 1400 mg orally twice daily (without ritonavir) or 1400 mg orally once daily plus ritonavir 200 mg once daily or 1400 mg orally once daily plus ritonavir 100 mg once daily or 700 mg orally twice daily plus ritonavir 100 mg twice daily Protase inhibitor-experienced adults: 700 mg orally twice daily plus ritonavir 100 mg twice daily
Sustaire(theophylline) extended release tablet *Branded generic product discontinued; other generic theophylline products are available	Look	100 mg, 300 mg	Not available.

Appendix H: Orthographic similarity and/or potential overlap in dose

Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Lusedra (fospropofol disodium)	**1,050 mg/30 mL vial (35 mg/mL)**	**Initial intravenous bolus dose of 6.5 mg/kg followed by supplemental dosages of 1.6 mg/kg as needed**
Luveris (lutropin alfa) injection 75 international units/vial	Orthographic similarity ('Luse' vs. 'Luve')	Wrong drug *Rationale:* Lusedra is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. In contrast, the dose of Luveris is 75 international units administered subcutaneously concomitantly with 75 to 150 international units of Gonal-f. Although you could obtain a 75 mg supplemental dose of Lusedra, this would be the dose for a five kilogram patient and Lusedra is only indicated for adults 18 years of age and older.
Lutera (levonorgestrel 0.1 mg/ethinyl estradiol 0.02 mg) + 7 placebo tablets	Orthographic similarity (both names begin with 'Lu' and have similar letters 'edra' vs. 'tera')	Wrong drug *Rationale:* Lusedra is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. In contrast, Lutera is likely to be prescribed without a strength.
Lysodren (mitotane) tablets 500 mg	Orthographic similarity ('Lused' vs. 'Lysod')	Wrong drug *Rationale:* Lysodren is an oral anticancer drug. The dose is 2 to 6 grams orally per day in divided doses, either 3 or 4 times a day. In contrast, Lusedra is administered intravenously for sedation during diagnostic or therapeutic procedures. Lusedra is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. Although dose could overlap, the different route of administration and the conditions of use (i.e., for sedation during procedures), will help differentiate the two products.

Lunesta (eszopiclone) tablets 1 mg, 2 mg, 3 mg	Orthographic similarity ('Lus' vs. 'Lun' and 'edra' vs. 'esta')	Wrong Drug *Rationale:* Lusedra is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. In contrast, the starting dose of Lunesta is 2 mg orally immediately before bedtime. Thus, the doses do not overlap.
Lustra Lustra AF Lustra Ultra (hydroquinone) cream, 4% Family of depigmenting creams	Orthographic similarity ('Lusedr' vs. 'Lustr')	Wrong drug *Rationale:* Lusedra is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. In contrast, no numerical dose is required for the Lustra products because it is applied topically to the affected area.
Lucentis (ranibizumab) injection, 10 mg/mL vial	Orthographic similarity ('Lused' vs. 'Lucent')	Wrong drug *Rationale:* Lusedra is administered intravenously for sedation. It is individually dosed based on the patient's weight (6.5 mg/kg). Supplemental doses (1.6 mg/kg) are administered as needed based on the level of sedation required. Lucentis is an ophthalmologic product. It is administered via intravitreal injection to treat macular degeneration. The dose of Lucentis is 0.5 mg, which is lower than any of the doses of Lusedra and thus decreases the potential for confusion.

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