

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022036Orig1s000

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: March 2, 2010

To: Russell Katz, MD, Director
Division of Neurology Products

Through: Melina Griffis, RPh, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Irene Z. Chan, PharmD, BCPS, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Silenor (Doxepin HCl) Tablets 3 mg and 6 mg

Application Type/Number: NDA 022036

Applicant: Somaxon Pharmaceuticals, Inc.

OSE RCM #: 2010-201

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

CONTENTS

1 INTRODUCTION.....	2
2 METHODS AND RESULTS.....	2
3 CONCLUSIONS AND RECOMMENDATIONS.....	2
4 REFERENCES.....	3
APPENDICES.....	4

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to a notification that NDA 022036 is anticipated to be approved within 90 days. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Silenor, acceptable in OSE Review #2008-96, dated October 23, 2008, OSE Review #2008-1941, dated February 9, 2009, and OSE Review # 2009-1294, dated November 19, 2009. The Division of Neurology Products did not have any concerns with the proposed name, Silenor, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on December 18, 2008.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria that were used in OSE Reviews #2008-96, #2008-1941, and #2009-1294 for the proposed proprietary name, Silenor. DMEPA was informed that the 1 mg strength will not be approved; therefore, we re-evaluated previous names of concern since any changes in the product characteristics of the proposed drug can affect our assessment. Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded four new names, Actemra, (b) (4), Solzira^{***}, and (b) (4)^{***}, thought to look similar to Silenor and represent a potential source of drug name confusion. These names were evaluated using FMEA. The findings of the FMEA indicate that the proposed name, Silenor, is not likely to result in name confusion with Actemra, (b) (4), Solzira^{***}, or (b) (4)^{***} for the reasons presented in Appendices A and B.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Silenor, as of February 3, 2010. Additionally, re-evaluation of previous names of concern did not identify any new concerns due to the change in product characteristic.

3 CONCLUSIONS AND RECOMMENDATIONS

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

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

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. **OSE review #2008-96 Proprietary Name Review of Silenor; Lee, Jinhee J.**
2. **OSE review #2008-1941 Proprietary Name Review of Silenor; Lee, Jinhee J.**
3. **OSE review #2009-1294 Proprietary Name Review of Silenor; Chan, Irene Z.**
4. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)
Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and “Chemical Type 6” approvals.
5. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)
USAN Stems List contains all the recognized USAN stems.
6. ***Division of Medication Error Prevention and Analysis proprietary name requests***
This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

Appendix A: Proposed proprietary name that has never been marketed in the U.S.

Proprietary Name	Similarity to Silenor	Description	Disposition of Name
Solzira ^{***} (Gabapentin Enacarbil) Tablets			(b) (4)
(b) (4)			

Appendix B: Product with no overlap in strength, dosage form, or route of administration

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Additional Comments
Silenor	N/A	1 mg, 3 mg, 6 mg	Take one tablet by mouth within 30 to 60 minutes of bedtime. Do not take with or immediately after a meal.	
Actemra (tocilizumab) Injectable	Orthographic	80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL	4 mg/kg intravenous infusion every four weeks followed by an increase to 8 mg/kg based on clinical response	(b) (4)
				(b) (4)

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22036	ORIG-1	SOMAXON PHARMACEUTICA LS INC	SILENOR (DOXEPIN HCL)

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

/s/

IRENE Z CHAN
03/02/2010

MELINA N GRIFFIS
03/02/2010

DENISE P TOYER
03/04/2010



**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: February 9, 2009

To: Russell Katz, MD, Director
Division of Neurology Products

Thru: Kellie Taylor, PharmD, MPH, Team Leader
Denise Toyer, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis

From: Jinhee J. Lee, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name: Silenor (Doxepin HCl) Tablets 1 mg, 3 mg, and 6 mg

Application Type/Number: NDA # 22-036

Applicant: Somaxon Pharmaceuticals, Inc.

OSE RCM #: 2008-1941

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

1 INTRODUCTION

This memorandum is in response to a request from the Division of Neurology Products for final review of the proprietary name, Silenor. This name was last reviewed on October 23, 2008 and found acceptable (OSE review 2008-96) but a review is necessary since more than 90 days have passed since the date of our last review.

2 PRODUCT INFORMATION

Silenor (Doxepin HCl) is a selective histamine H₁ antagonist indicated for the treatment of insomnia, as demonstrated by improvement in sleep onset, sleep maintenance and ^{(b) (4)}

 Silenor will be available in 1mg, 3 mg, and 6 mg strength immediate-release tablets.

3 DISCUSSION

During our re-review of the proposed proprietary name, Silenor, the Division of Medication Error Prevention and Analysis (DMEPA) identified 12 names not previously reviewed in OSE review 2008-96 (listed Appendix A) and we determined that the 12 identified names were unlikely to result in medication errors with Silenor. Therefore, we have concluded that the proprietary name Silenor is acceptable for this product.

4 CONCLUSIONS AND RECOMMENDATIONS

We have completed our review of the proposed proprietary name, Silenor, and have concluded that it is acceptable. However, if the product is delayed beyond 90 days from the date of this memorandum, the proposed name must be resubmitted for evaluations.

DMEPA 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 Applicant with regard to this review. If you have further questions or need clarifications, please contact Daniel Brounstein, OSE Project Manager, at 301-796-0674.

Appendix A: Additional names identified and reason to discard

Name	Similarity to Silenor	Reason to Discard
Celestone	Sound	Different strength (0.6 mg/5 mL), dosage form (oral solution), and dosage (0.6 mg to 7.2 mg daily)
Gilenia ^{***}	Look	(b) (4)
Selanir	Look and Sound	Proprietary name for Cefaclor in Italy that is no longer marketed
Sevelamer	Look	Name lacks convincing orthographic similarities
Siderol	Look	Different strength [multiple vitamin with minerals (no strength) – nutraceutical]
Sildec	Look	Name lacks convincing orthographic similarities
Silence	Look	Marketed in Hong Kong
Silentan	Look	Proprietary name for Nefopam HCL in Germany that is no longer marketed Proprietary name for diazepam, dihydroergotamine tartrate, aspirin, and caffeine in Switzerland that is no longer marketed
Silver Sulfadiazine	Sound	Name lacks convincing phonetic similarities
Soltamox	Look	Name lacks convincing orthographic similarities
Tylenol	Sound	Name lacks convincing phonetic similarities
Zolinza	Look	Different strength (100 mg) and dosage (300 mg to 400 mg daily)

^{***} Proprietary and confidential information that should not be released to the public.***

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

/s/

Jinhee Lee
2/10/2009 02:31:03 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
2/13/2009 01:29:35 PM
DRUG SAFETY OFFICE REVIEWER



**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: October 23, 2008

To: Russell Katz, Director
Division of Neurology Products

Thru: Kellie Taylor, PharmD, MPH, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Jinhee J. Lee, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name, Label, and Labeling Review

Drug Name: Silenor (Doxepin HCl Tablets) 1 mg, 3 mg, and 6 mg

Application Type/Number: NDA # 22-036

Applicant: Somaxon Pharmaceuticals, Inc.

OSE RCM #: 2008-96

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

Contents

EXECUTIVE SUMMARY	3
1 BACKGROUND	3
1.1 Introduction.....	3
1.2 Regulatory History	3
1.3 Product Information	3
2 METHODS AND MATERIALS	3
2.1 Proprietary Name Risk Assessment	4
2.2 Label and Labeling Risk Assessment	9
3 RESULTS.....	10
3.1 Proprietary Name Risk Assessment.....	10
3.2 Label and Labeling Risk Assessment	11
4 DISCUSSION	12
4.1 Proprietary Name Risk Assessment.....	12
4.2 Label and Labeling Risk Assessment	12
5 CONCLUSIONS AND RECOMMENDATIONS	14
5.1 Comments to the Division.....	14
5.2 Comments to the Applicant.....	14
6 REFERENCES	16
7 APPENDICES	17

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.¹

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Silenor, 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, Silenor, the medication error staff of DMEPA search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). DMEPA also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.3).

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 2.1.3). 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.² 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. DMEPA uses 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, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

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.

¹ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

³ 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 ‘S’ 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 Silenor, 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 (7 letters), up-strokes (2, capital letter ‘S’, ‘1’), down-strokes (none), cross-strokes (none), and dotted letters (1, “i”). Additionally, several letters in Silenor may be vulnerable to ambiguity when scripted, including the letter ‘S’ may appear as ‘A’, or ‘L’; lower case ‘o’ appear as a lower case ‘a’, and ‘n’ as ‘m’. As such, the Staff should also consider these alternate appearances when identifying drug names that may look similar to Silenor.

When searching to identify potential names that may sound similar to Silenor, the medication error staff search for names with similar number of syllables (3), stresses (SI-len-or or si-LEN-or or si-len-OR), vowel sound pronunciation (“Sil” versus “Sile”), and placement of vowel and consonant sounds. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Silenor. The Applicant’s intended pronunciation of the proprietary name is “SI-leh-nor” and was taken into consideration when identifying potential names.

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 (Silenor), the established name (doxepin HCl), proposed indication (treatment of insomnia), strength (1 mg, 3 mg, and 6 mg), dose (1 mg to 6 mg), frequency of administration (once daily at bedtime), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff general take into consideration.

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 Databases and Information Sources

The proposed proprietary name, Silenor, was provided to the medication error staff of DMEPA 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 Silenor using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To 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.

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)

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Silenor. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of DMEPA 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 External Proprietary Name Risk Assessment

For this product, the Applicant submitted an independent risk assessment of the proposed proprietary name conducted by a third party consulting firm. DMEPA conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's staff database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

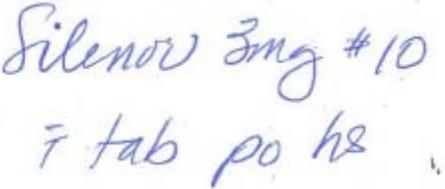
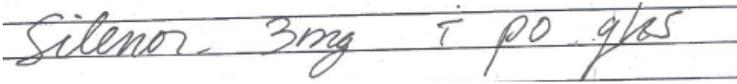
After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Sponsor. The Safety Evaluator then determines whether DMEPA's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, DMEPA provides a detailed explanation of these differences.

2.1.3 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Silenor 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 125 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 Silenor 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 125 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. Silenor Study (conducted on February 14, 2008)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> 	<p>Silenor 3 mg 1 tablet by mouth at bedtime.</p>
<p><u>Inpatient Medication Order :</u></p> 	

2.1.4 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, DMEPA 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 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 Silenor 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 Silenor 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

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

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.

DMEPA 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. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
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 DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA 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 IOM, WHO, JCAHO, and ISMP, 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, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, 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, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

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

2.2 LABEL AND LABELING RISK ASSESSMENT

This section describes the methods and materials used by DMEPA Staff to conduct a label, labeling, and/or packaging risk assessment (see Section 3, Results). The primary focus of the assessments is to identify and remedy potential sources of medication errors prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.⁷

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container label and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the United States Pharmacopeia-Institute for Safe Medication Practices Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁸

Because DMEPA staff analyzes reported misuse of drugs, DMEPA staff is able to use this experience to identify potential errors with all medications similarly packaged, labeled or prescribed. DMEPA uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provide recommendations that aim at reducing the risk of medication errors.

DMEPA reviewed the following labels and labeling submitted by the Applicant on August 29, 2008. See Appendices H through J for pictures of the labels and labeling.

- Commercial Container Labels
- Blister Trade Packs
- Sample Physician Blister Packs
- Package Insert Labeling (no image)

⁷ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁸ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

- Patient Labeling (no image)

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Databases and Information Sources

DMEPA's searches identified 18 names as having some similarity to the name Silenor.

Nine of the 18 names were thought to look like Silenor, which include: Saluron, Salagen, Kelnor, (b) (4) Soliris, Simcor, Selsun, Silenil, and Silexin. Three names (Zaditor, Dilor, and Zelapar) were found to sound like Silenor, and six names (Zelnorm, Selenor, Selenos, Selenium, Silenor, and Sular) were thought to look and sound similar to Silenor.

As of July 30, 2008, the proposed name, Silenor, did not contain a U.S. Adopted Name (USAN) stem.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1.1. above) and did not have any additional comments. The Expert Panel recommended that the AERS database be searched for name confusion with the existing product.

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

3.1.3 FDA Prescription analysis studies

A total of 28 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 86% of the participants (n=24) interpreted the name correctly as "Silenor". All four misinterpretations occurred in the phonetic prescription study with the prefix interpreted as "Sel-" and "Cyl-" in two cases and the suffix interpreted as "-nove" in one case. The middle vowel, "e", was interpreted incorrectly in all four cases as "a" or "i". See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 External Name Studies

In the proposed name risk assessment submitted by the Applicant, the (b) (4) commissioned two separate studies (i.e. physician study and pharmacist study) that evaluated the applicability, acceptability, and validation of the proposed proprietary name. Their study participants included a total of 30 physicians and 10 retail-based pharmacists.

Six participants (20%) in the physician study associated Silenor with the following drugs: Sominex (1 mention), Sonata (1 mention), Zelnorm (1 mention), Singulair (1 mention), and Micronor (2 mentions). We note that the (b) (4) stated that "more than two thirds of the respondents did not associate Silenor with any other brand", however, we were not provided with the remaining \pm 4 participant responses. We question what these responses were and whether they are different than the other responses submitted. Additionally, it does not appear that the identified names were further evaluated by the (b) (4) as no further detail was provided about these findings.

In the pharmacist study, 30% of the respondents stated that Silenor phonetically reminded them of Tylenol because they each had three syllables with a "specific emphasis on the first syllable with 'similar' sounding second syllable". However, the (b) (4) did not find Tylenol to be problematic given their varying indications, medication classes, and prescription versus OTC status.

Five names identified by the (b) (4) were not previously identified in the DMEPA Staff searches, the Expert Panel Discussion, or FDA prescription studies.

3.1.5 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Independent searches by the primary Safety Evaluator identified four additional names (Silinove, Xylonol, Xylonol, and (b) (4)) thought to look and/or sound similar to Silenor and represent a potential source of drug name confusion. As such, a total of 27 names were analyzed to determine if the drug names could be confused with Silenor and if the drug name confusion would likely result in a medication error.

Twelve of the names lacked orthographic and phonetic similarity and were eliminated from further evaluation (Appendix C). The remaining 15 names were determined to have some orthographic and/or phonetic similarity to Silenor, and thus determined to present some risk for confusion.

Failure Mode and Effects Analysis was then applied to determine if the proposed name, Silenor, could potentially be confused with any of the 15 names and lead to medication error. This analysis determined that the name similarity between Silenor and the identified names was unlikely to result in medication errors for all 15 products for reasons described/outlined in Appendices D through G.

3.2 LABEL AND LABELING RISK ASSESSMENT

3.2.1 General Comments

Review of the container labels, carton and insert labeling identified several potential sources of medication error.

The product strengths appear above the proprietary name in conjunction with the net quantity.

The labels and labeling for the 3 mg and 6 mg strengths look similar.

The drug product is packaged in a “unit of use” bottle.

The established name does not appear at least ½ the size of the proprietary name.

3.2.2 Commercial Container Labels (1 mg, 3 mg, 6 mg)

See General Comments.

The Applicant name appears in a font size that competes with the established name.

3.2.3 Commercial Blister Carton Labeling (1 mg, 3 mg, 6 mg)

See General Comments and section 3.2.2.

3.2.4 Sample Blister Carton Labeling (4 tablet and 7 tablet)

See General Comments and section 3.2.2.

A “per tablet” statement is not present on the carton labeling.

The labeling for the 7 count blister cartons look similar for all three strengths.

3.2.5 Package Insert Labeling

No comments.

3.2.6 Patient Labeling

No comments.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

A total of 27 proprietary names were assessed using FMEA. Our findings indicate the proposed name Silenor does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, DMEPA believes that these limitations are sufficiently minimized by the use of an Expert Panel, the CDER Prescription Studies that involved 125 CDER practitioners, and, in this case, the data submitted by the Applicant from an independent proprietary name risk assessment firm, which included the responses of frontline practitioners.

4.2 LABEL AND LABELING RISK ASSESSMENT

Our Label and Labeling Risk Assessment noted several areas of needed improvement.

4.2.1 *Position of Strength*

The strength typically appears immediately following the established name. However, in its current presentation, the strength appears above the proprietary name and adjacent to the net quantity statement. It would be preferable and in alignment with standard label/labeling layout if the strength followed the proprietary and established names.

4.2.2 *Differentiation of Strength*

The Applicant has taken steps to use different font colors for each of the three Silenor strengths. However, the 3 mg and 6 mg strengths have overlapping colors (i.e. white, blue, and gray) in the fill, the outline, or the background. Additionally, the proprietary and established names (i.e. Silenor and Doxepin HCl) have an identical blue and white background that increases the visual similarity of the two strengths, making it difficult to differentiate the two strengths from each other (see pictures below in Figure 1). In order to decrease the potential for selection error, we suggest using different color schemes for the strengths.

Figure 1



4.2.3 Prominence of Established Name

Although the font size of the established name appears ½ the size of the proprietary name, it does not have a prominence commensurate with the prominence of the proprietary name. It does not take into account all pertinent factors, including typography, layout, contrast, and other printing features. The disparity in size may be attributed to the outlining of the proprietary name which increases the prominence of the name. Thus, this presentation does not meet 21 CFR 201.10(g)(2).

4.2.4 Prominence of Company Logo

The Applicant's name competes with the presentation of the established name on the container labels and blister carton labeling and appears more prominent (See Figure 2 below). Competing with the prominence of the proprietary and established names is problematic because it is distracting and diverts one's attention from the drug product name. The proprietary and established names should be the most prominent items on the labels and labeling to minimize this distraction and the Applicant name should be reduced in stature.

Figure 2



4.2.5 Child Resistant Closure

It is unclear whether the 30 tablet bottles have a Child Resistant Closure (CRC). Since 30 tablets is considered a unit-of-use bottle based on the dosing of this product, we need to ensure that the cap is CRC to be in accordance with the Poison Prevention Packaging Act (PPPA) of 1970.

4.2.6 Blister Labeling

We note that the 4 and 7 tablet blister card labeling does not include a "per tablet" statement. Our post-marketing surveillance has demonstrated that omitting this statement is a source of confusion as patients are misled to believe that the entire contents of the blister equate to the stated strength dose. In other words, we are concerned that patients will take all 4 or 7 tablets thinking it equaled to the milligram amount of Silenor expressed on the blister.

4.2.7 Blister Label

The proprietary and established names are present on the principal display panel where the tablets will be located, however, the product strength is not. Our post-marketing evidence has shown that patients separate tablets/capsules from the blister packaging because it is less bulky to carry. If a patient has multiple strengths of Silenor without the strengths displayed on the packaging, it is easy to see how an inadvertent substitution may take place. Thus, it is important to have the proprietary and established names in addition to the product strength for identification purposes and to minimize the occurrence of inadvertent strength substitution should this panel be separated from the rest of the blister carton.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Silenor, is not vulnerable to name confusion that could lead to medication errors. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant. Thus, DMEPA has no objection to the use of the name, Silenor, for this product. Additionally, DDMAC does not object to the proposed name, Silenor, from a promotional perspective. However, if **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed blister and pouch labels and carton labeling introduces vulnerability to confusion that could lead to medication errors. Specifically, DMEPA notes problems with the prominence, presentation, and consistency of information that is vital to the safe use of the product. DMEPA believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

5.1 COMMENTS TO THE DIVISION

We 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 DMEPA on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Daniel Brounstein, OSE project manager, at 301-796-0674.

5.2 COMMENTS TO THE APPLICANT

A. Proprietary Name

DMEPA has no objections to the use of the proprietary name Silenor for this product. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and the name must be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the date of our review, the proposed name will be re-reviewed.

B. All Labels and Labeling

1. Relocate the strength so that it appears below the proprietary and established names so that it is in alignment with standard label/labeling layout.
2. Although the font size of the established name appears ½ the size of the proprietary name, it does not have a prominence commensurate with the prominence of the proprietary name. It does not take into account all pertinent factors, including typography, layout, contrast, and other printing features. Revise the labels and labeling in accordance with 21 CFR 201.10(g)(2).
3. The color schemes of the 3 mg and 6 mg strengths look similar. Revise the color of the fill, the outline, and/or the background ensuring that the revised color schemes do not overlap with each other.
4. Ensure that the unit-of-use bottles have a Child Resistant Closure (CRC) per the Poison Prevention Packaging Act to avoid accidental ingestion of Silenor.

C. Container and Blister Labels and Blister Carton Labeling

1. Reduce the font size of your company logo so that it does not compete with the prominence of the established name.
2. Include a “per tablet” statement for each of the sample blister carton labeling packs to avoid confusion and a resulting drug misadventure where a patient ingests the total contents.
3. Insert the product strength wherever the proprietary and established names are present on the blister carton labeling. If the panels with the tablets are separated from the rest of the blister carton packaging, the omission of this pertinent information may increase the potential of an inadvertent ingestion of an unintended strength.

6 REFERENCES

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

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

2. ***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 and Analysis, FDA.

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

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

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

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

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

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

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

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

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

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

Provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** (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.

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

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

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

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

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

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.

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

List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

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

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

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

16. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

7 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. DMEPA 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 (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, DMEPA 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, DMEPA 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 Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix C: Names that lack convincing orthographic and/or phonetic similarities

Name	Similarity to Silenor
Salagen	Look
Soliris	Look
Selsun	Look
Zaditor	Sound
Dilor	Sound
Zelapar	Sound
Sular	Look and Sound
Tylenol	Sound
Singulair	Look and Sound
Micronor	Look and Sound
Sominex	Look and Sound
Sonata	Look and Sound

Appendix D: Products with information not available.

Name	Similarity to Silenor
(b) (4)	Look
(b) (4)	Look and Sound

Appendix E: Proprietary names used in Foreign Countries

Name	Similarity to Silenor	Country
Selenor	Look and Sound	Poland
Silenor ^{***}	Look and Sound	Trademark registration pending in Canada and Mexico. Trademark registered in Europe.
Silenil	Look	Poland
Silinove	Look and Sound	France
Xylonor	Sound	Spain
Xylonol	Sound	Taiwan

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

Product name with potential for confusion	Similarity to Silenor	Strength and Dosage Form	Usual Dose (if applicable)
Silenor (Doxepin HCl)		1 mg, 3 mg, 6 mg Tablets	Usual dose: 1 mg to 3 mg, taken 30 to 60 minutes before bedtime.
Saluron (Hydroflumethiazide)	Look	50 mg Tablets	<u>Edema</u> : 50 mg daily or twice daily to start, then 25 mg to 200 mg daily. <u>Hypertension</u> : 50 mg twice daily to start, then 50 mg to 100 mg per day up to 200 mg per day.
Kelnor (Ethinyl Estradiol/Ethinodiol Diacetate)	Look	0.035 mg/1 mg Tablets	1 tablet daily.
Simcor (Niacin/Simvastatin)	Look	500 mg/200 mg, 750 mg/20 mg, 1000 mg/20 mg Extended-release Tablets	1000 mg/20 mg to 2000 mg/40 mg once daily.
Silexin (Guafenesin/Dextromethorphan HBr) – OTC	Look	100 mg/10 mg per 5 mL Syrup	2 teaspoonfuls every 4 hours
Selenos (Selenium Sulfide)	Look and Sound	2.25% Shampoo	Apply to wet scalp and massage in. Leave on for 2-3 minutes. Rinse thoroughly. Two applications per week for 2 weeks usually brings to control.

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

			After 2 weeks, the shampoo may be used less frequently as needed.
Selenium (Selenium)	Look and Sound	50 mcg, 100 mcg, 200 mcg Tablets 40 mcg/mL (10 mL) Injection Solution	Metabolically stable: 20 mcg to 40 mcg daily. Deficiency from prolonged TPN support: 100 mcg/day for 24 and 31 days.

Appendix G: Potential confusing name with numerical overlap in strength or dose

Silenor (Doxepin HCl)	1 mg, 3 mg, 6 mg Tablets	Usual dose: 1 mg to 3 mg, taken 30 to 60 minutes before bedtime.
Failure Mode: Name confusion	Causes (could be multiple)	Effects
Zelnorm (Tegaserod)	<p>Orthographic similarity (The middle letters in Zelnorm, “-el-nor-” resemble “-ilenor” in Silenor. Both have a similar number of letters (six versus seven).</p> <p>Phonetically, the first letters, “Z” and “S”, and the first syllable vowel sounds, “-el-” and “-il-” as well as the suffixes “-norm” and “-nor” sound similar when pronounced.</p> <p>Both have an overlapping strength (6 mg), dosage form (tablet), and route of administration (oral).</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 risk for medication error is minimized by the orthographic differences in the names. The “Z” in Zelnorm is distinct from the “S” in Silenor when written. When spoken, Silenor has an additional syllable and Zelnorm ends with the letter “m” which helps to differentiate the two names from each other.</p> <p>Moreover, the sales and marketing of Zelnorm was suspended following a request from the FDA. This suspension resulted from a number of cardiovascular-related adverse events reported by users. However, Zelnorm has a restricted distribution for use in Investigational New Drug (IND) protocols. Thus, it is very unlikely that even if Silenor were to be misinterpreted as Zelnorm, that the wrong medication would be dispensed.</p> <p>Despite some overlapping product, orthographic, and phonetic characteristics, we believe the risk for medication error to be minimal given the restricted distribution of Zelnorm, the differences in the orthographic appearance of the first letters, and the additional syllable in Silenor.</p>

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

/s/

Jinhee Lee
10/24/2008 08:45:49 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/24/2008 01:40:56 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/24/2008 03:42:37 PM
DRUG SAFETY OFFICE REVIEWER